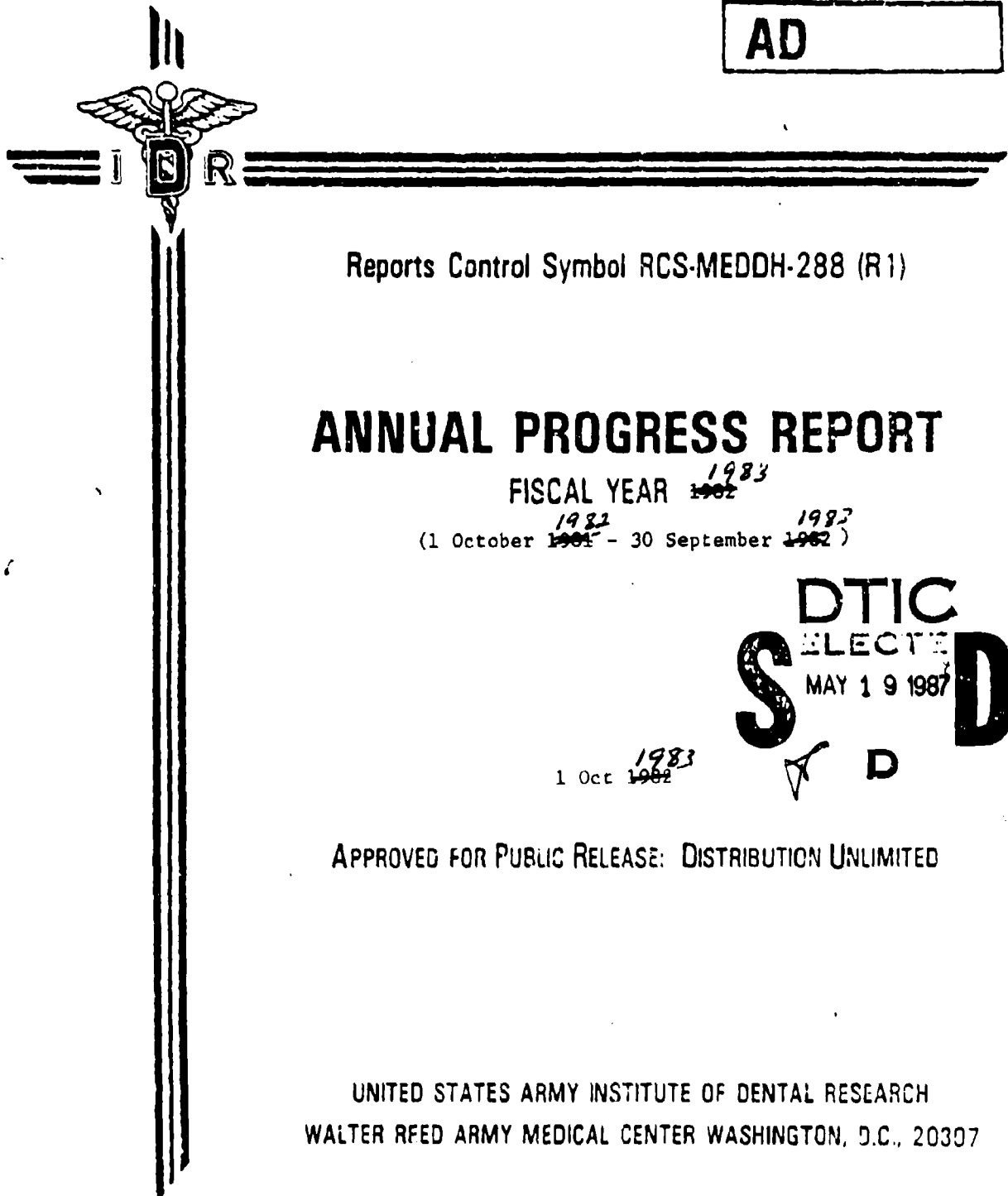


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(1 October ¹⁹⁸²~~1981~~ - 30 September ¹⁹⁸³~~1982~~)

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UNITED STATES ARMY INSTITUTE OF DENTAL RESEARCH
WALTER REED ARMY MEDICAL CENTER WASHINGTON, D.C., 20307

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UNITED STATES ARMY INSTITUTE OF DENTAL RESEARCH
WALTER REED ARMY MEDICAL CENTER
WASHINGTON, DC 20307-5300

ANNUAL REPORT
(1 October 1982-30 September 1983)

Thomas P. Sweeney, COL, DC

October 1983

Supported by

US ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21701-5012

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WALTER REED ARMY MEDICAL CENTER
WASHINGTON, DC 20307-5300

ANNUAL PROGRESS REPORT

1 October 1982 - 30 September 1983

DA Project	3A161101A91C	00	<u>In-House Laboratory Research</u>
DA Project	3M161102BS10	Task DA	<u>Management of Dental Injury & Combat Dentistry</u>
DA Project	3S162775A825	Task AA, AB, AC, AD	<u>Combat Maxillofacial Injury</u>
DA Project	3M162734A875	Task AQ	<u>Medical Defense Against Chemical Agents</u>

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
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19. KEY WORDS (Continue on reverse side if necessary and identify by block number) (U) Ancillary Personnel; (U) Antimicrobial Agents; (U) Aphthous Stomatitis; (U) Base Metal Alloys; (U) Biocompatible; (U) Biodegradable; (U) Biodegradable Copolymer; (U) Biopolymers; (U) Bonding Agents; (U) Bone; (U) Bone Stimulating; (U) Casting Accuracy; (U) CD-1 Mice; (U) Cellulose Triacetate;		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) DA Project 3M161102BS10 Management of Dental Injury and Combat Dentistry - Task DA The objectives are to obtain information by the techniques of clinical and basic research on injuries and diseases, except communicable diseases, commonly seen in soldiers, especially in field operations and overseas. The work is divided according to the major dental specialties. Emphasis is placed on diseases and injuries that are receiving little or no study by ————over		

BLOCK 19. Continued:

(U) Ceramic; (U) Ceramic Block; (U) Cidex; (U) Citric Acid; (U) Cold Weather Survey; (U) Composite Restoratives; (U) Controlled Release; (U) Copolymer; (U) Copolymer Bandage; (U) Corrosion of Alloys; (U) Cranio-Mandibulofacial Complex; (U) Crevicular Fluid; (U) Cyclic AMP; (U) Dental Cutting Instrument; (U) Dental Emergencies; (U) Dental Identification; (U) Dental Materials; (U) Dental Porcelain; (U) Dental Radiology; (U) Dental X-ray; (U) Diphosphoinoside-Lysozyme; (U) Dogs; (U) DOT-ELISA; (U) Foreign Bodies; (U) Gentamicin; (U) Gingival Exudates; (U) Gingival Trauma; (U) Granular Tricalcium Phosphate; (U) Guinea Pigs; (U) Health Services Research; (U) Herpetic Lesions; (U) Hydroxyproline; (U) Immunology; (U) Immunopathology; (U) Implant; (U) Impression Materials; (U) Indomethacin; (U) Infection Control; (U) Inflammation; (U) Inhibition; (U) Inhibition of Bone Resorption; (U) Interceptive Methods; (U) Intermaxillary Fixation; (U) Investment Techniques; (U) Isobutyl 2-Cyanoacrylate; (U) Krebs's Cycle Derivatives; (U) Laboratory Animal; (U) Laser Reflectance; (U) Lidocaine; (U) Lip Pathology; (U) Liver Surgery; (U) Logistic Models; (U) Lymphocytes; (U) Lymphokine; (U) Marginal Leakage; (U) Materiel; (U) Medical Materiel; (U) Mice; (U) Microbiology; (U) Microencapsulation; (U) Microencapsulated Antibiotics; (U) Monoclonal Antibodies; (U) Nerve Agent; (U) New Bone Formation; (U) Opaque Porcelain; (U) Operations Research; (U) Oral Health Status; (U) Organ Culture; (U) Osseous; (U) PGE; (U) PLA/PGA Covering; (U) Polypentapeptide; (U) Porcelain-Metal Bond; (U) Post and Core Restorations; (U) Predictive Methods; (U) Prostaglandin; (U) Rabbits; (U) Radioisotope; (U) Radionuclide X-ray System; (U) RAM IV; (U) Rapid Detection; (U) Rats; (U) Recurrent Aphthous Stomatitis; (U) Recurrent Oral Ulceration; (U) Resin Restorative; (U) Rhesus Monkey; (U) Salivary Amylase; (U) Salivary Enzyme; (U) Salivary Physiology; (U) Segmental Mandibular Defects; (U) Serrated; (U) Shelf-Life; (U) Soldering Base Metals; (U) Sporidicin; (U) Storage Stability; (U) Subtraction Radiography; (U) Sustained Release Antibiotic; (U) Tissue Adhesive; (U) Tooth; (U) Tracheal Grafts; (U) Tricalcium Phosphate; (U) Tumorigenicity Study; (U) Ultrasound; (U) Volunteers; (U) Wound Dressing; (U) Wound Exudate; (U) Wound Healing; (U) Wound Infection; (U) Xerocheilitis; (U) X-ray Portable

BLOCK 20 Continued:

civilian research groups, and the work is aimed at providing better preventive measures as well as treatment.

DA Project 3S162775A825 Combat Maxillofacial Injury.)

Tasks AA, AB

The objectives are to develop simplified procedures for the care of complex maxillofacial wounds and injuries which require long time-consuming procedures for reconstruction; to achieve minimal morbidity rates from oral emergencies, preventable oral disease, and restorative failures; and to develop more efficient, simplified, effective clinical and laboratory techniques which will result in better utilization of manpower and a saving in time and materiel.)

DA Project 3M162734A875 Medical Defense Against Chemical Agents.)

Task AQ

The objectives and purposes are the development of the basic scientific data required for systems of soldier CW agent antidotes, soldier/patient decontamination, and medical management of CW casualties. Research: Copolymers;

Gingival Trauma; Rhesus Monkey;

Shall I say medicine ←

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FOREWORD

IN CONDUCTING THE RESEARCH DESCRIBED IN THIS REPORT, THE INVESTIGATORS ADHERED TO THE "GUIDE FOR THE CARE AND USE OF LABORATORY ANIMALS" AS PREPARED BY THE COMMITTEE ON CARE AND USE OF LABORATORY ANIMALS OF THE INSTITUTE OF LABORATORY ANIMAL RESOURCES, NATIONAL RESEARCH COUNCIL.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				DATE: 01 OCT 83		REPORT CONTROL SYMBOL: 201708	
1. NAME OF WORK UNIT		2. WORK UNIT TYPE		3. WORK UNIT STATUS		4. WORK UNIT CLASSIFICATION	
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81101A		JA181101A91C		00		815	
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12. CROSS ORJ. NONE							
13. TITLE OF WORK UNIT (Include "Research and Technology Work Unit" in title)							
(U) CONTROLLED RELEASE OF ANTIGENS FOR ONE-DOSE IMMUNIZATION							
14. WORKING AND TECHNICAL AREAS		15. ESTIMATED COMPLETION DATE		16. FUNDING AGENCY		17. FUNDING METHOD	
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(U) LAB ANIMALS ; (U) RATS ; (U) MICROENCAPSULATION ; (U)							
35. CONTROLLED RELEASE: (U) IMMUNIZATION							
<p>OBJECTIVE: (U) IT IS THE TECHNICAL OBJECTIVE OF THIS WORK TO DETERMINE THE FEASIBILITY OF APPLYING CONTROLLED RELEASE OF MULTIPLE VACCINE ANTIGENS OF A PREPROGRAMMED MANNER SO THAT A HIGH TITER ANTIBODY RESPONSE IS ELICITED IN THE HOST. SUCCESSFUL DEVELOPMENT OF THE UNIVERSAL VACCINE WOULD RESULT IN A ONE-DOSE, ONE-STEP IMMUNIZATION PROCEDURE FOR SERVICE PERSONNEL.</p> <p>APPROACH: (U) A BIOCOMPATIBLE, BIODEGRADABLE POLYMER POLY (DL-LACTIDE-CO-GLYCOLIDE), WILL BE USED TO COAT DISPERSED PARTICLES OF OPT VACCINE. MICROSPHERES GREATER THAN 250 M WILL BE FORMULATED SINCE THEY ARE INJECTABLE THROUGH A CONVENTIONAL HYPODERMIC NEEDLE. THE RATE OF ANTIGEN RELEASE WILL BE CONTROLLED BY PROPER CHOICE OF POLYMER AND SYSTEM DESIGN. THE IMMUNE RESPONSE TO THE ENCAPSULATED ANTIGENS WILL BE MONITORED AND COMPARED TO CONVENTIONALLY IMMUNIZED CONTROLS. A SUCCESSFUL IMMUNE RESPONSE TO THE OPT (DIPHTHERIA, PERTUSSIS, TETANUS) ANTIGENS WOULD ENCOURAGE INCORPORATION OF ADDITIONAL VACCINE ANTIGENS. IT IS ANTICIPATED THAT THE QUANTITY OF ANTIGEN NEEDED TO STIMULATE THE DESIRED IMMUNE RESPONSE WILL BE CONSIDERABLY LOWER THAN THAT REQUIRED WHEN ADMINISTERED CONVENTIONALLY. IT IS POSSIBLE THAT THE POLYMER WILL HAVE AN ADJUVANT EFFECT THAT MAY ENHANCE THE IMMUNE RESPONSE.</p> <p>PROGRESS: (U) NONE.</p>							

PROJECT: 3M161102BS10

WORK UNIT TITLE: (U) Acceleration of Wound Healing

PRINCIPAL
INVESTIGATOR: LTC Jeffrey O. Hollinger, DC

A Study on the Behavior of Bone in Organ Culture with Special
Emphasis on PGE₂ and Indomethacin

PROBLEM: It has been demonstrated that PGE₂ administered to bone implants results in an increase in osteoclasts and decrease in total bone volume. Cyclic AMP (cAMP) has been described in relation to prostaglandins (PG) and bone resorption (Yu *et al.*, 1979). Cyclic GMP (cGMP) has been mentioned as a possible antagonist of cAMP (Elattar, 1978). It is fundamentally important to understand the principles of bone resorptive processes and agents that control or buffer those activities so that osteolysis can be controlled and bone morbidity can be decreased.

APPROACH: Calvaria were removed aseptically from CD-1, 5-7 day old neonatal mice and were placed into tissue culture wells containing enriched BGJ₁ medium. Calvaria were divided equally into control and treatment groups of 4 calvaria per group. The treatment groups had either a known or putative PGE₂ inhibitor added to the medium (i.e., indomethacin, phenylbutazone). All calvaria were incubated at 37°C in 5% CO₂ and air. Specimens were retrieved at 24, 48, and 72 hours and were assayed by ¹²⁵I-RIA for PGE₂, c-AMP, and c-GMP; and by atomic absorption spectroscopy for Ca++ concentration.

RESULTS: The per cent PGE₂ and Ca++ differences between treatment and control groups were used as bench marks for comparisons. The indomethacin (100ng/ml) displayed several levels of prostaglandin E₂ inhibition during the 72 hour test period. Maximum levels for indomethacin and niflumic acid were 98% and 80%, respectively. Phenylbutazone levels must be reconfirmed, as they were variable. Cyclic AMP levels of experimental calvaria were greater than control. The greatest increase (5 times control) occurred in PGE₂ supplemental media. The smallest increase (1 1/2 times control) took place in the niflumic acid supplemental media. Cyclic GMP levels, however, varied in their relation to control and experimental. The ratio of c-AMP/c-GMP ranged from 6/1 (24 hours) to 67/1 (72 hours) for PGE₂ medium. Other experimentally supplemented media exhibited temporal variations of c-AMP/c-GMP which were less drastic. Cyclic AMP increased in approximately a parabolic fashion and c-GMP decreased in approximately linear fashion in the PGE₂ medium. Relationships between c-AMP and c-GMP displayed an approximately non-sloping, linear relationship with all other experimental media. Results may be summarized by stating that known and probable inhibitors that were evaluated affected PGE₂ synthesis in vitro; however, certain inhibitors (i.e., indomethacin) caused almost complete PGE₂ inhibition and may, therefore, prove to be useful in controlling osteolysis in vivo. Furthermore, in vitro the presence of PGE₂ is associated positively

with c-AMP and inversely with c-GMP. Similar associations between cAMP, cGMP, and PG inhibitors were not demonstrated.

PROJECT: 3M161102BS10

WORK UNIT TITLE: (U) Acceleration of Wound Healing

PRINCIPAL
INVESTIGATOR: LTC Jeffrey O. Hollinger, DC

A Study on 50:50 PLA:PGA Plus Diphosphoinositide-Lysozyme (DPI-L)
for the Promotion of Calcification in Osseous Healing

PROBLEM: To determine if a biodegradable, biocompatible copolymer of PLA and PGA in combination with a diphosphoinositide inositol-lysozyme complex could induce osteogenesis in experimental wounds created in endochondral and intramembranous bones.

APPROACH: A material was formulated that consisted of a combination of a proteolipid and biodegradable, biocompatible copolymer. The proteolipid was prepared by combining a lysozyme and phosphatidyl inositol 4, 5 - diphosphate in a 1:1 weight ratio. A raw polymer of 50:50 poly (L(-) lactide-co-glycolide) was solubilized in methylene chloride, reprecipitated with anhydrous methanol, and blended with the proteolipid at a 1% w/w ratio of proteolipid to copolymer. The combined material was formed into cylindrical implant plugs (1.95mm X 2.05mm) in a teflon mold and placed into a lyophilizer chamber for 48 hours at 40°C. The implants recovered were then sterilized with ethylene oxide for 6 hours and degassed. Implants were also prepared that consisted of only a plain copolymer of 50:50 poly (L(-) lactide-co-glycolide), and these were managed in a fashion identical to the copolymer plus proteolipid. One hundred and eighty rats were randomly divided into three groups and wound sites were prepared in the tibias using a bone trephine (1.95mm O.D.). One group(A) received copolymer - proteolipid implants; the second group(B) received plain copolymer; the third group(C) served as controls. At 3, 7, 14, 21, 28, and 42 days animals from each group were sacrificed and implant sites were retrieved, processed for plastic embedding, stained by Goldner-trichrome, and 3.5 μ sections were evaluated histomorphometrically using an image analysis system. In addition to the tissue histomorphometry, serum and bone alkaline and acid phosphatases were assayed; protein and hydroxyproline determinations were performed; and atomic absorption spectrophotometric evaluations were done to quantify calcium and phosphate molar ratios in host bone. Isoelectric focusing was also applied for isoenzyme identification.

RESULTS: The copolymer-proteolipid implant group demonstrated overall increases in the total volumetric density of bone formation, trabecular diameter, osteoid thickness, and number of osteoblasts that exceeded the healing response in wounds of groups B and C. Similarly, the plain copolymer group results exceeded those of the control group. Overall trends between treatment groups displayed an ascending, predominantly linear difference over time; however, towards the latter stages a quadratic component of that trend was evident. Based solely upon histomorphometric data, therefore, it appears that the copolymer-proteolipid implant may be useful

for stimulating the important early phase of bone repair. Biochemical enzyme assays were an unpredictable indicator of osseous repair. In contrast, histochemical assays were considerably more representative and essentially the data on these analyses ran parallel to the histomorphometric variables. Atomic absorption spectrophotometry and isoelectric focusing proved to be of only marginal value in evaluating bone repair.

PROJECT: 3M161102BS10
WORK UNIT TITLE: (U) Acceleration of Wound Healing
PRINCIPAL
INVESTIGATOR: LTC Jaffrey O. Hollinger, DC

Enhanced Healing of Soft Tissue Wounds Using Diphenylhydantoin Sodium
Incorporated into a Meshwork of Biodegradable Copolymer
(50:50 poly L-(-) lactide-co-glycolide)

PROBLEM: To develop an agent that could be applied topically to a skin wound to hasten primary closure. To develop an agent that could "bulk-up" atrophic soft tissue morphology.

APPROACH: A fibrous mesh consisting of 50:50 poly L-(-) lactide-co-glycolide incorporating diphenylhydantoin-sodium (DPH) was prepared. An unembellished mesh (pure copolymer) was also prepared. Excisional wounds 3X5cm were made to the panniculus carnosus in backs of rats. Treatment consisted of either one or the other types of fibrous mesh dressing, IP - DPH, or no treatment. Wound sites were evaluated histologically, histomorphometrically, by total protein and hydroxyproline assays, by tensile testing, and by RIA (¹²⁵I) for DPH.

RESULTS: The 1-28 day evaluation period analyses revealed little or no difference between treatments for the excisional wounds. Subtle differences were occasionally displayed by animals receiving IP-DPH. This group displayed a greater amount of collagen and a higher density of fibroblasts than the other treatment groups. The primary reason for the lack of a positive healing response may be explained as a consequence of the "wicking" action that was engendered by the fibrous nature of the copolymer mesh. This condition militated against an intimate tissue-dressing interface, obviating suitable DPH dissemination into the healing wound bed. A second generation "film-type" dressing has been prepared; however, continuation of this project can no longer be anticipated.

PROJECT: 3M161102BS10
WORK UNIT TITLE: Acceleration of Wound Healing
PRINCIPAL
INVESTIGATOR: James R. Heath III

Identification of Leukocyte Populations Responsible
for Production of OAF and Their Role in Bone Resorption

PROBLEM: Studies have shown 10-12% of all combat wounds involve the maxillofacial apparatus. Many of these result in contaminated osseous wounds. The lymphokine, Osteoclast Activating Factor (OAF), is one of the mediators of the delayed bone healing seen in contaminated osseous wounds. OAF is produced by white blood cells in response to bacterial products and stimulates local osteoclasts leading to bone resorption instead of bone growth. A better understanding of the mechanisms of action of OAF and of its chemical nature could lead to an abrogation of the detrimental effects of OAF and thus an acceleration of wound healing.

APPROACH: 1. Production of OAF: OAF is produced in vitro by stimulating human small lymphocytes with the mitogen phytohemagglutinin (PHA) in large volume cell culture. The culture supernatants are filter sterilized then passed through an ultrafiltration membrane with a 10,000 molecular weight cut-off. The retentate is made 1 molar with NaCl and filter dialyzed with phosphate buffered saline (PBS) on the same membrane. The ultrafiltrate and dialysate are combined and subjected to a second ultrafiltration on a 1,000 molecular weight cut-off membrane followed by filter dialysis with PBS. The retentate is fractionated on a Sephadex G-25 packed column with PBS as the mobile phase.

2. Bioassays: (a) The presence of osteolytic activity in ultrafiltration fractions, culture supernatants, ultrafiltration retentates and filtrates is measured by the standard bone resorption bioassay. Briefly, rats in the 18th day of gestation are injected i.p. with ^{45}Ca . The following day, the fetuses are removed aseptically and the radial and ulnar bones of each fetus are dissected free of muscle, connective tissue and cartilaginous epiphyses and placed individually in 4 wells of a 24-well culture plate containing 0.23ml BGJ₁ in each well. After an 18hr preculture, the culture medium is removed and replaced with 0.125ml test solution and the other pair receives control solution. The bones are incubated for 120 hrs. at 37°C in 5% CO₂ and 100% humidity. The bones and culture supernatants are separated and placed in individual scintillation vials. The bones are decalcified with 5% CCl₃COOH and then the amount of ^{45}Ca in both bones and culture supernatants is determined. The per cent $^{45}\text{Ca}^{++}$ released from experimental and control bones is computed. A test/control (T/C) ratio is computed. T/C ratios >1 indicate increased bone resorption. However, ratios <1 are ambiguous since they could indicate either decreased bone resorption, increased calcium uptake or toxicity of the test solution to the bone culture. (b) To resolve the ambiguity seen when ratios >1 are encountered, we have developed the following modification of the standard

bioassay. The bones are not prelabeled with ^{45}Ca prior to dissection. Instead, an equal amount of ^{45}Ca is added to every well at the same time the test and control solutions are added. The incubation time is shortened to 6 hrs. The percent of calcium uptake is computed and a T/C per cent uptake determined. Thus, this modification is essentially a reversal of the standard bone resorption assay.

RESULTS: We have reported identifying a substance in the PHA stimulated human mononuclear cell culture supernatants which causes a highly significant inhibition of osteolysis in the bone resorption bioassay. Further studies in the past year have shown that this substance, in nanogram quantities can block the activity of the known osteolytic agents prostaglandin (PGE_2) and OAF. Using the new modification of the bone assay, we have found that this substance causes a significant ($p < .0001$) increase in calcium uptake. This accounts for the antiosteolytic activity of the substance and suggests that it may be a stimulator of osteogenesis.

PROJECT: 3M161102BS10

WORK UNIT TITLE: (U) Acceleration of Wound Healing

PRINCIPAL
INVESTIGATOR: COL Stephen G. Woodyard

Citric Acid Enhancement of Oral Soft Tissue Healing

PROBLEM: Citric acid application to uncontaminated root surfaces apparently enhances soft tissue healing. Soft tissue pedicle flaps do not heal satisfactorily when placed against contaminated tooth root surfaces as evidenced by a failure of such tissues to reattach. This investigation was designed to determine if citric acid applications might enhance soft tissue healing (adhesions) to contaminated root surfaces as might occur following oral wounding.

APPROACH: Single surface root recession defects were created in six monkeys followed by six weeks of exposure to oral fluids. Surgical repair utilizing soft tissue flaps placed against citric acid treated and untreated root surfaces followed. Histologic evidence of repair was evaluated.

RESULTS: Citric acid application significantly enhanced wound repair, indicating this treatment offers substantial benefit. Adhesion of tissue allowed nearly complete repair of exposed root surfaces to be accomplished, unlike control surfaces where repair was unsatisfactory.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ABBREVIATION		2. DATE OF SUMMARY		REPORT CONTROL SYMBOL	
				DA OP 6021		83 10 01		DD-DRG-2(A)136	
3. DATE PREPARED	4. DATE OF SUMMARY	5. SUMMARY TYPE	6. WORK SECURITY	7. ABBREVIATION	8. ABBREVIATION	9. ABBREVIATION	10. ABBREVIATION	11. ABBREVIATION	12. ABBREVIATION
82 10 01	82 10 01	U	U						
13. NO./CODES		14. PROGRAM ELEMENT		15. PROJECT NUMBER		16. TASK AREA NUMBER		17. WORK UNIT NUMBER	
61102A		3M161102BS10		DA		010			
18. CONTRIBUTING		19. CONTRIBUTING		20. CONTRIBUTING		21. CONTRIBUTING		22. CONTRIBUTING	
23. TITLE (Provide and Security Classification Code)		24. TITLE (Provide and Security Classification Code)							
		(U) Problems Involved in Military Oral Health Care Delivery Related to Therapeutic Agents and Materials							
25. SCIENTIFIC AND TECHNOLOGICAL AREA		26. SCIENTIFIC AND TECHNOLOGICAL AREA							
012600 Pharmacology		002300 Biochemistry 010100 Microbiology							
27. DATE		28. DATE		29. DATE		30. DATE		31. DATE	
68 09		CONT		DA		C. IN-HOUSE			
32. CONTINUED/REVIEW		33. CONTINUED/REVIEW		34. CONTINUED/REVIEW		35. CONTINUED/REVIEW		36. CONTINUED/REVIEW	
37. DATE/EFFECTIVE		38. DATE/EFFECTIVE		39. DATE/EFFECTIVE		40. DATE/EFFECTIVE		41. DATE/EFFECTIVE	
42. NUMBER		43. NUMBER		44. NUMBER		45. NUMBER		46. NUMBER	
47. TYPE		48. TYPE		49. TYPE		50. TYPE		51. TYPE	
52. NAME OF AWARD		53. NAME OF AWARD		54. NAME OF AWARD		55. NAME OF AWARD		56. NAME OF AWARD	
57. ABBREVIATION FOR ORGANIZATION		58. ABBREVIATION FOR ORGANIZATION		59. ABBREVIATION FOR ORGANIZATION		60. ABBREVIATION FOR ORGANIZATION		61. ABBREVIATION FOR ORGANIZATION	
USA Institute of Dental Research		USA Institute of Dental Research		USA Institute of Dental Research		USA Institute of Dental Research		USA Institute of Dental Research	
ADDRESS: Washington, DC 20307		ADDRESS: Washington, DC 20307		ADDRESS: Washington, DC 20307		ADDRESS: Washington, DC 20307		ADDRESS: Washington, DC 20307	
RESPONSIBLE INDIVIDUAL		RESPONSIBLE INDIVIDUAL		RESPONSIBLE INDIVIDUAL		RESPONSIBLE INDIVIDUAL		RESPONSIBLE INDIVIDUAL	
NAME: SWEENEY, T.P.		NAME: SWEENEY, T.P.		NAME: SWEENEY, T.P.		NAME: SWEENEY, T.P.		NAME: SWEENEY, T.P.	
TELEPHONE: 202 576-3484		TELEPHONE: 202 576-3484		TELEPHONE: 202 576-3484		TELEPHONE: 202 576-3484		TELEPHONE: 202 576-3484	
62. GENERAL USE		63. GENERAL USE		64. GENERAL USE		65. GENERAL USE		66. GENERAL USE	
Foreign Intelligence Considered		Foreign Intelligence Considered		Foreign Intelligence Considered		Foreign Intelligence Considered		Foreign Intelligence Considered	
67. REVIEWED (Provide and Security Classification Code)		68. REVIEWED (Provide and Security Classification Code)		69. REVIEWED (Provide and Security Classification Code)		70. REVIEWED (Provide and Security Classification Code)		71. REVIEWED (Provide and Security Classification Code)	
72. TECHNICAL OBJECTIVE		73. TECHNICAL OBJECTIVE		74. TECHNICAL OBJECTIVE		75. TECHNICAL OBJECTIVE		76. TECHNICAL OBJECTIVE	
23. (U) To evaluate the special military problems of drug storage, heat susceptibility, long-term drug potency, sterility of bulk items, lack of refrigeration in combat zones and delivery to the patient. To investigate drug hazards. To investigate the use of biodegradable polymers for the long-term, slow release of drugs.		24. (U) Improved means of drug delivery in the field using microencapsulated medications will be studied. The hazards in the use of various drugs and the use of biodegradable, biocompatible materials for surgical repair of combat wounds will be studied.		25. (U) 8209-8309 Ampicillin anhydrate microcapsules have been formulated using a 50:50 PL-PLGA excipient. The goal was achieved when highly loaded microcapsules with desired in vivo release kinetics were obtained in very good yields. The microcapsules were effective in vivo. Problems remain in the formulation of gentamicin sulfate microcapsules. Although release kinetics are not optional, the drug has been encapsulated in 50:50 DL-PLG.					

PROJECT: 3M161102B810

WORK UNIT TITLE: (U) Problems Involved in Military Oral Health Care
Delivery Related to Therapeutic Agents and
Materials

PRINCIPAL
INVESTIGATOR: JEAN A. SETTERSTROM, Ph.D.

Development of Encapsulated Antibiotics for Topical
Administration to Wounds

Problem: Combat wounds are characterized by a high incidence of infection primarily because of the inevitable presence of devitalized tissue and foreign body contaminants from missile fragments that carry dirt and debris into the wound. During evacuation, the wound may be exposed to further contamination and delay before initial treatment. Wound healing in the combat casualty, therefore, must overcome adversities not seen in the highway victim or civilian counterpart. Among soldiers, infections have remained a major cause of morbidity that results in lengthened hospitalization and combat ineffectiveness.

Approach: Improved methods to deliver antibiotics to contaminated tissue following traumatic injury are needed in order that sustained and effective tissue levels of antibiotics can be maintained at the wound site despite the inadequate perfusion of blood resulting from shock or the destruction of blood vessels to devitalized areas. The improved method should be easily applied in a single dose to the wound site as soon as possible after injury when infection is most likely to be suppressed. Such a novel antibiotic delivery system is being developed in which ampicillin anhydrate and gentamicin sulfate are being incorporated individually into microspheres of biocompatible, biodegradable, copolymer that are formulated to slowly release the drug over a sustained period (14 days). These microspheres, which will completely biodegrade once all drug is released, exist as a free-flowing powder that can be easily dusted onto wounds under field conditions.

Results: Experiments were performed to evaluate the efficacy of prototype microcapsules in artificially induced infections. Wounds 2.5-3.0cm long and 1cm deep were made in the thigh muscle of albino rats. The muscles were traumatized by uniformly pinching with tissue forceps, and inoculated with known quantities of Staphylococcus aureus and Streptococcus pyogenes. Sterile dirt was placed in each wound to serve as an infection potentiating factor. The wounds were then treated within one hour by sprinkling sterile, preweighed amounts of microencapsulated antibiotic directly in the wound. Control groups consisted of animals with wounds receiving no therapy, unloaded microcapsules, or topically applied, free ampicillin anhydrate. All

wounds were sutured closed with 3-0 black silk.

The ampicillin anhydrate microcapsules effectively reduced bacterial counts in the contaminated wounds. S. pyogenes was present in 90% of the untreated wounds at 14 days, but was eliminated from microcapsule treated wounds within 48 hours. Although S. aureus remained in all microcapsule treated wounds at 7 days, compared with untreated controls, the bacterial count decreased ($>2 \log_{10}$ /gram of tissue) between day 2 and 7. This reduction was not observed in untreated controls. Wounds treated with unloaded DL-PGL microcapsules, or topically applied free ampicillin anhydrate remained infected at 14 days with $\geq 10^5$ organisms per gram of tissue. Whereas, 60% of the wounds treated with microencapsulated ampicillin anhydrate were sterile.

Successful controlled release of bioactive ampicillin anhydrate was achieved in vitro and in vivo. The system developed provides a successful model that encourages efforts to encapsulate additional antibiotics. Often, it may be desirable for broad spectrum control to combine two or more antibiotics in treating wounds. It is anticipated that mixtures of different antibiotic-containing microcapsules may be blended and packaged together to increase the versatility of the product.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION ^a	2. DATE OF SUMMARY ^a	REPORT CONTROL SYMBOL	
				DA OF6024	831001	DD-DM&F(AR)636	
3. DATE PREVIOUS ^a	4. KIND OF SUMMARY	5. SUMMARY ICT ^a	6. WORK SECURITY ^a	7. RESEARCH ^a	8. DMRN INST ^a	9. SPECIFIC DATA CONTRACTOR ACCESS	10. LEVEL OF SUM
821001	H. TERM	U	U		NL	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	A. WORK UNIT
11. NO./CODES ^a	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER			
A. PRIMARY	61102A	3M161102BS10	DA	012			
B. CONTRIBUTING							
C. CONTRIBUTING	/ / / / /	STOG 82/83-6.2:4					
11. TITLE (Provide DM Security Classification Code)							
(U) Identification and Control of Oral Infections							
12. SCIENTIFIC AND TECHNOLOGICAL AREAS ^a							
010100 Microbiology; 002300 Biochemistry; 012600 Pharmacology							
13. START DATE		14. ESTIMATED COMPLETION DATE		15. FUNDING AGENCY		16. PERFORMANCE METHOD	
6607		CONT		DA		C. IN-HOUSE	
17. CONTRACT/GRANT				18. RESOURCES ESTIMATE		19. PROFESSIONAL MAN YRS	
A. DATES/EFFECTIVE:				B. PRESENT		C. FUNDS (in thousands)	
B. NUMBER ^a				FISCAL YEAR		83	
C. TYPE:				CURRENCY		2.0	
D. KIND OF AWARD:						15.4	
E. AMOUNT:							
F. CUM. AMT.							
20. RESPONSIBLE ORG ORGANIZATION				21. PERFORMING ORGANIZATION			
NAME ^a U S Army Institute of Dental Research				NAME ^a U S Army Institute of Dental Research			
ADDRESS ^a Washington, DC 20307				ADDRESS ^a Washington, DC 20307			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Provide SSAN if U.S. Academic Institution)			
NAME: SWEENEY, T.P.				NAME ^a SETTERSTROM, J.A.			
TELEPHONE: (202) 576-3484				TELEPHONE: (202) 576-2290/3662			
				SOCIAL SECURITY ACCOUNT NUMBER: POC:DA			
22. GENERAL USE				ASSOCIATE INVESTIGATORS			
Foreign Intelligence Considered				NAME: Woodyard, S.			
				NAME: Vincent, J., Heath, J.			
23. (U) Oral Health Status; (U) Gingival Exudates; (U) Cravicular Fluid; (U) Sporidini; (U) Cidex; (U) Monoclonal Antibodies							
23. (U) To investigate the source and treatment of orofacial infections encountered in field conditions, foreign countries and diverse climates. To evaluate the special agents, instruments and chemicals necessary under military conditions.							
24. (U) Orofacial infections of significance in the diverse military environment will be studied by microbiological, immunological, and electron microscopy methods. Possible sources of oral infections will be evaluated and the effectiveness of commercially available as well as in-house designs will be studied for their ability to control or prevent oral infections.							
25. (U) Several <u>in vivo</u> evaluations of wound dressings containing povidone iodine and benzalkonium chloride have been performed. To date, all experiments have suggested that while these antiseptic agents can decrease somewhat the bacterial counts in the wound, they do not reach an acceptable level at 72 hours. An <u>in vitro</u> evaluation of the effectiveness of nitrofurazone resulted in similar findings. At present, steps are underway to evaluate clindamycin, ampicillin, and chlorhexidine diphenylate in the same wound dressing material. Studies have begun on the production and use of monoclonal antibodies for the rapid identification of maxillofacial infections. The similarity of cellular protein patterns has been determined by polyacrylamide gel electrophoresis. Hybridoma cells producing antibody reactive with <u>Fusobacterium nucleatum</u> have been cloned and antibody produced and purified from mouse ascites fluid. Steps are underway to accomplish this for the five other anaerobic microorganisms selected for study.							

^a Available to contractors upon originator's approval

DD FORM 1498

PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. (DD FORM 1498, 1 FEB 74, AND 1 FEB 75, 1 MAR 76 FOR ARMY USE) ARE OBSOLETE.

PROJECT: 3M161102BS10

WORK UNIT TITLE: (U) Identification and Control of Oral Infections

PRINCIPAL
INVESTIGATOR: COL Jack W. Vincent, DC

In Vivo Evaluation of a Dressing Containing Poly-L(-)

Lactide and Povidone Iodine

PROBLEM: In a battlefield environment, the feasibility of immediate evacuation of a patient may not exist. Wounds which are contaminated or which run the risk of contamination will require an effective means of therapy for extended periods. Antimicrobial agents presently must be administered on a continuing basis which may not be advantageous in a hostile environment. If wound infection is not prevented or controlled, the detrimental effects which hinder the healing process may become life threatening or, at the least prolong recovery time before the soldier can return to duty.

APPROACH: A wound dressing of a non-woven poly-L(-) lactide has been developed. This material has been shown to be able to incorporate both povidone iodine and benzalkonium chloride and once incorporated, to release this material in a controlled fashion over a 72 hour period in vitro. This determination involved release into a reservoir of buffer. This study was designed to evaluate these materials in vivo to determine if the release kinetics were the same and, if so, were these preparations effective in treating an infected wound. The guinea pigs were selected as the animal model due to the anatomical similarity of the subcutaneous tissue of the paravertebral area in relation to that of a humans. A controlled size full thickness wound created in this area would receive a known quantity of a known pathogen. This area would then be covered with a wound dressing containing the antimicrobial agent to be tested. An identical wound receiving the same inoculum will be covered with the same wound dressing without the antimicrobial agent and thus serve as a control. Following application, the wound dressing will be secured in place with tissue adhesive. After 72 hours all wounds will be assayed for viable microorganisms from the initial inoculum. Tissue biopsies can be removed, homogenized and resulting supernatant assayed for cfu/mg tissue weight. An alternate means of assay will be to isolate the wound surface with a sterile wash-basin and scrubbing the surface with a mild detergent solution. This solution can then be evaluated by serially diluting and plating on culture medium to determine cfu/ml which can be converted to cfu/surface area. Bacterial counts of 10^5 cfu (or greater)/cm² is indicative of an infected wound.

RESULTS: During this period, several in vivo experiments have been accomplished in order to evaluate these antimicrobial agents. Initially thirty guinea pigs (twenty experimental and ten control) were wounded by full thickness dissection in the paravertebral area inoculated with

approximately 10^9 /ml of Staphylococcus aureus following which they were covered with the appropriate wound dressings: ten controls, ten containing povidone iodine and ten containing benzalkonium chloride. Following 72 hours incubation, tissue biopsies were removed, homogenized and assayed. Counts from both experimental groups were low ($0-10^5$ cfu/gm) however, counts were also low in the control group animals ($0-10^7$ cfu/gm). The possibility of absorption of the inoculum into the non-woven dressing was a distinct possibility which although possibly a good characteristic for a wound dressing did little to allow evaluation of the efficiency of the antimicrobial agent involved. This experiment was repeated and at the time of assay, the wound dressing material was also evaluated for viable S. aureus. Both the experimental and control dressing demonstrated high counts of S. aureus indicating the inability of povidone iodine to control this organism. Pure povidone iodine (22mg/cm² wound) also proved ineffective in the management of this wound model. At this time by a standard tube dilution method for its ability to inhibit the growth of S. aureus in vitro. A concentration of 6.2 g/ml inhibited visible growth of S. aureus however, when this material was plated, high counts were obtained even from samples containing 50 g/ml of nitrofurazone. These results suggest that nitrofurazone would not be effective in this model system. Efforts are presently being directed toward characterization of non-woven dressing powders and microcapsules containing clindamycin, ampicillin, and chlorhexidine diphosphanilate.

PROJECT: 3M161102BS10

WORK UNIT TITLE: (U) Identification and Control of Oral Infections

PRINCIPAL

INVESTIGATOR: COL Jack W. Vincent, DC

Production and Utilization of Monoclonal Antibodies in the
Rapid Identification of Anaerobic Microorganisms Associated With
Maxillofacial Infections

PROBLEM: There is currently no rapid method for the identification of microorganisms present in a wound exudate. Conventional techniques require approximately 2 to 3 days for this procedure. Such a delay in evaluating contaminated maxillofacial wounds and in selecting appropriate antibiotic therapy could result in severe sequelae. A method of rapid detection would appear to be ideal for the prevention of such a delay and may serve as a model for the detection of biological agents which might be utilized in a biological warfare environment.

APPROACH: The technique of monoclonal antibodies will be used to develop a system for the rapid identification of anaerobic microorganisms. A 2% suspension of whole cells of bacteria will be used to immunize BALB/c BYJ mice by an intraperitoneal injection (0.25ml) weekly for five weeks. At three days before the cell fusion a final injection will be given to each mouse. After anesthesia, the spleen will be removed aseptically and minced to a single cell suspension and residual red blood cells lysed by the addition of 0.17M ammonium chloride. Approximately 10^8 splenocytes will be combined with either 10^6 P-3 mouse myeloma cells or 10^6 P-3 Ag 8.653 mouse myeloma cells in the presence of 35% polyethylene glycol to allow for fusion and then plated in a selective medium which will inhibit the growth of all but successfully fused hybrid cells. These hybrids will be screened by serological methods so as to identify clones of cells which carry the genetic information enabling synthesis and secretion of monoclonal antibody and, also, the ability to survive in cell culture. Appropriate hybrid clones will be isolated by limiting dilution and grown in sufficient volume so as to be preserved in cryoprotective media. Following isolation, these clones can be injected (10^6 viable cells) intraperitoneally into BALB/c mice which have been previously primed with pristane. The ascites fluid produced by the resulting tumors should contain 25-75mg/ml of antibody. When isolated this monoclonal antibody will be used to develop a system for rapid (2-3 hours) detection of wound contaminants. Such a system (most probably the ELISA) must display extreme sensitivity and specificity which should be provided by these techniques.

RESULTS: BALB/c BYJ mice have been immunized with the following anaerobic microorganisms: Fusobacterium nucleatum, Bacteroides gingivalis, Bacteroides fragilis, Peptococcus magnus, Peptostreptococcus micros and Peptostreptococcus anaerobius. Both the cell lines P-3 and P-3 Ag 8.653 have

been used for fusion procedures. To date several fusion attempts have been destroyed by fungal growth or by failure of the selective medium to inhibit the growth of unfused cells. To date, a hybrid cell line containing nuclear material from splenocytes sensitized to F. nucleatum and P-3 mouse myeloma cells has been cloned and shown to be positive for anti - F. nucleatum antibody by ELISA. Additional fusions have been performed using other splenocytes and P-3 Ag 8.653 mouse myeloma cells. Preliminary results suggest hybrid cells have resulted which are producing antibody reactive with Peptococcus magnus and Bacteroides fragilis. Work is presently ongoing to accomplish these same procedures with the remaining anaerobic microorganisms selected for study.

PROJECT: 3M161102BS10

WORK UNIT TITLE: (U) Identification and Control of Oral Infections

PRINCIPAL
INVESTIGATOR: COL Jack W. Vincent, DC

Use of Monoclonal Antibodies for the Isolation and Identification
of Osteoclast Activating Factor (OAF) and a Recently
Identified Inhibitor of Osteolysis

PROBLEM: The study of OAF presently requires a prolonged procedure in order to obtain the material from the culture supernatant of stimulated human leukocyte. Once obtained in the form of 105, 5ml fractions, each fraction must be tested in a bone bioassay system in order to identify OAF activity. A maximum of 15 fractions/week can be tested. In addition, there is presently no technique which can be used to identify OAF in tissue specimens or to determine its site of activity. When available, monoclonal antibodies could be utilized in vivo to block OAF activity much in the same way as they are presently used to block graft vs host reactions in bone marrow transplants.

APPROACH: The technology of monoclonal antibodies can be utilized due to their specificity or ability to recognize and react with a single antigenic determinant when present in a vast mixture of substances. Mice which have been immunized with the antigen of interest provide sensitized lymphoblasts which, in the presence of polyethylene glycol, can be fused with an established mouse myeloma cell line. Resulting hybrid cell lines carry nuclear material from both cells thus are coded for synthesis and secretion of monospecific antibodies and the capability of survival in continuous culture. Although OAF is a small molecule (molecular weight 1500 daltons) for an effective immunogen, other small molecules can be detected by antibody reactions. If it is possible to develop monoclonal antibodies to OAF, such antibodies could be used to extract OAF from crude culture supernatants by affinity chromatography. Such a capability could be accomplished in days rather than the months now required to fractionate and test culture supernatants acquired from phytohemagglutinin (PHA) stimulated human leukocyte populations. These antibodies could also be used to identify the specific active site of OAF in tissue specimens. Lastly, as anti-T-cell monoclonal antibodies vs host responses with bone marrow transplants in immuno-deficient hosts, anti-OAF antibodies could be used to control or eliminate OAF activity in vivo. An additional substance whose biological activity appears to be one of inducing osteogenesis has also been identified in these same culture supernatants of stimulated human leukocytes. The activity of this substance is such that it can apparently block OAF activity and the activity of other known osteolytic agents when evaluated with a molecular weight of 6000 daltons requires the identical, lengthy procedures for isolation and identification as does OAF. Monoclonal antibodies reactive with this substance would provide the same advantages as

those previously described for OAF.

RESULTS: A crude culture supernatant from a PHA stimulated human leukocyte culture was tested to verify both OAF and the osteolytic inhibitor activity. The crude form was utilized in the hopes that these substances might be present in a complex form which might prove to be more immunogenic. An additional sample of culture supernatant was mixed with bovine serum albumin (BSA) (1mg/ml) because of the known tendency of OAF to complex with BSA and thus take advantage of a more complex and more immunogenic substance. On a weekly basis for five weeks two BALB/c BYJ mice were infected intraperitoneally with 0.25ml of this complex. Fusion of splenocytes obtained from these mice was performed three days following the final immunization. Approximately 10^6 splenocytes and 10^6 P-3 mouse myeloma cells were exposed to 35% polyethylene glycol and then plated in a selective medium which would inhibit the growth of all but hybrid cells. Following twenty-one days of incubation, twenty-four hybrid clones were detected and transferred to larger volume culture. When viability counting identified the presence of at least 5×10^6 cells, the clones were transferred to a cryoprotective medium and frozen for preservation in liquid nitrogen at a concentration of 5×10^6 cells per ml. Testing for specificity was accomplished by an inhibition assay combined with the bone bioassay. Due to technical problems, only samples of the osteolytic inhibitors were available. This 6000 molecular weight fraction would also contain some OAF as this 1500 molecular weight substance is known to exist in complexed forms in the mol. wt. range of 1500 to 18,000 daltons. The inhibition assay involved incubation of the osteolytic inhibitors with the culture supernatant from hybrid clones prior to the bone bioassay with the same osteolytic inhibitors incubated with uninoculated culture medium served as appropriate controls. Of the hybrids tested, none appeared to inhibit the activity of the osteolytic inhibitor but four hybrid clones appeared to enhance the osteogenic effect. It is speculated that this phenomenon may represent an inactivation of residual OAF in this fraction. These hybrid clones are preserved and available for testing against OAF at this time.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				REPORT CONTROL SYMBOL	
DA302808		01 OCT 83		Z01708	
A NEW		U		U	
10. NO. CODES: PROGRAM ELEMENT		PROJECT NUMBER		TASK AREA NUMBER	
61102A		3M1811028310		DA 081	
11. FORMER					
12. TITLE: ORJ 5700: 82/83-E 2/B					
(U) IDENTIFICATION OF LEUKOCYTE POPULATIONS RESPONSIBLE FOR PRODUCTION OF OSTEOCLAST ACTIVATING FACTOR AND THEIR ROLE IN BONE RESORPTION					
002300 BIOCHEMISTRY		002800 BIOLOGY		010200 MINING	
OCT 83		CONT		C. IN-HOUSE	
13. DATES: EFFECTIVE		14. RESOURCES: ESTIMATE		15. PROFESSIONAL: MAN. YRS	
16. NUMBER		17. POSITION		18. FLAMES: IN. TAILORING	
19. TIME		20. YEAR		21. YEAR	
22. END OF AWARD		23. CUM/TOT		24. S. O	
25. REPORTING: NO. ENCL. 70-104		26. REPORTING: NO. ENCL. 70-104		27. REPORTING: NO. ENCL. 70-104	
28. NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR		29. NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR		30. NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR	
31. ADDRESS: WASHINGTON DC 20307		32. ADDRESS: WASHINGTON DC 20307		33. ADDRESS: WASHINGTON DC 20307	
34. RESPONSIBLE: NAME & S.		35. RESPONSIBLE: NAME & S.		36. RESPONSIBLE: NAME & S.	
37. NAME: SWEENEY, T P		38. NAME: HEATH, J R. III		39. NAME: HEATH, J R. III	
40. TELEPHONE: 202-578-3484		41. TELEPHONE: 202-578-3082		42. TELEPHONE: 202-578-3082	
43. COUNTRY: P. I. C. A.		44. COUNTRY: P. I. C. A.		45. COUNTRY: P. I. C. A.	
46. MILITARY: (U) IN APPLICATION		47. MILITARY: (U) IN APPLICATION		48. MILITARY: (U) IN APPLICATION	
49. MILITARY: (U) IN APPLICATION		50. MILITARY: (U) IN APPLICATION		51. MILITARY: (U) IN APPLICATION	
(U) WOUND HEALING (U) OSTEOCLAST ACTIVATING FACTOR (U) LYMPHOKINE (U) BONE RESORPTION (U) LAB ANIMALS (U) RATS (U) RAM IV:					
<p>OBJECTIVE: (U) MAXILLOFACIAL WOUNDS ACCOUNT FOR 10-12 PERCENT OF ALL COMBAT WOUNDS. MANY OF THESE RESULT IN CONTAMINATED OSSEOUS WOUNDS. THE LYMPHOKINE OSTEOCLAST ACTIVATING FACTOR (OAF) IS ONE OF THE AGENTS THAT CAUSES THE DELAYED BONE HEALING SEEN IN THIS TYPE OF WOUND. A BETTER UNDERSTANDING OF THE ACTION AND CHEMICAL NATURE OF OAF COULD LEAD TO AN ABROGATION OF ITS DETRIMENTAL EFFECTS ON BONE HEALING AND THUS LEAD TO AN ACCELERATION OF BONE HEALING.</p> <p>APPROACH: (U) OAF IS PRODUCED BY STIMULATING HUMAN LEUKOCYTES WITH THE MITROGEN PHYTOHEMAGGLUTININ (PHA) IN LARGE VOLUME CELL CULTURE. THE CULTURE SUPERNATANTS, WHICH CONTAIN OAF IN NANOGRAM QUANTITIES, ARE FIRST SUBJECTED TO AN ULTRAFILTRATION PROTOCOL WHICH CONCENTRATES AND ISOLATES COMPOUNDS WITH MOLECULAR WEIGHTS BETWEEN 1,000 AND 10,000 DALTONS. THIS IS FOLLOWED BY GELFILTRATION ON A STANDARDIZED COLUMN. OAF IS DETECTED IN CULTURE SUPERNATANTS AND PURIFICATION FRACTIONS BY A STANDARD BONE RESORPTION BIOASSAY WHICH INVOLVES THE RELEASE OF SUPERSCRIP 45CA FROM FETAL RAT LONG BONES IN VITRO. THIS PROJECT WAS STARTED AS DA088037.</p> <p>PROGRESS: (U) NONE.</p>					

00 1400M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				PROJECT IDENTIFICATION		REPORT CONTROL NUMBER	
				DA302928		01 OCT 83	
						VE0208	
1. TYPE OF WORK		2. TYPE OF WORK		3. TYPE OF WORK		4. TYPE OF WORK	
A. NEW		U		U		CX	
10. NO./CODES		PROGRAM ELEMENT		PROJECT NUMBER		TASK AREA NUMBER	
61102A		3M111028510		DA		384	
11. CONTINUING							
12. CONTINUING							
13. TITLE (PROJECT OR TASK OR SUBPROJECT OR SUBTASK)							
(U) MONOCLONAL ANTIBODIES FOR THE ISOLATION AND IDENTIFICATION OF OSTEOCLASTIC ACTIVATING FACTOR (OAF) & A RECENTLY IDENTIFIED INHIBITOR OF OSTEOLYSIS							
14. SUBJECT AREA AND GROUP							
0818 PHYSIOLOGY				0813 MICROBIOLOGY			
15. START DATE		16. ESTIMATED COMPLETION DATE		17. FUNDING ORGANIZATION		18. FUNDING METHOD	
OCT 83		CONT		DA		C. IN-HOUSE	
19. JUSTIFICATION				20. RESOURCES ESTIMATE			
a. GATES PROJECT		b. GATES PROJECT		c. PROFESSIONAL WORK YEARS		d. FUNDS (i.e. \$ thousands)	
1983		1984		0.6		\$ 0	
1984				0.8		\$ 24	
21. FUNDING ORIGIN		22. FUNDING ORIGIN		23. FUNDING ORIGIN		24. FUNDING ORIGIN	
F. GUM/TOT		S. O		038876		H100	
NAME MORDC INSTITUTE OF DENTAL RECH USAIDR				NAME MORDC INSTITUTE OF DENTAL RECH USAIDR			
ADDRESS WASHINGTON DC 20307				ADDRESS WASHINGTON DC 20307			
RESPONSIBLE INDIVIDUAL				RESPONSIBLE INDIVIDUAL			
NAME SWEENEY, T P				NAME VINCENT, J W			
TELEPHONE 202-878-3484				TELEPHONE 202-878-3082			
25. SPECIAL USE				26. SPECIAL USE			
MILITARY				MILITARY			
27. COUNTRY ORIGIN (FOR U.S. CITIZENSHIP PURPOSES)				28. COUNTRY ORIGIN (FOR U.S. CITIZENSHIP PURPOSES)			
(U) IMMUNOLOGY ; (U) MONOCLONAL ANTIBODIES ; (U)				(U) IMMUNOLOGY ; (U) MONOCLONAL ANTIBODIES ; (U)			
LYMPHOKINES ; (U) LAB ANIMALS ; (U) MICE ; (U) RAB IV				LYMPHOKINES ; (U) LAB ANIMALS ; (U) MICE ; (U) RAB IV			
29. OBJECTIVE (U) CONTAMINATION OF AN OSSEOUS WOUND OF THE MAXILLOFACIAL COMPLEX WOULD RESULT IN MITROGENIC STIMULATION OF THE HOST'S IMMUNE SYSTEM. ONE OF THE RESULTANT BIOLOGICALLY ACTIVE SUBSTANCES PRODUCED WOULD BE OAF WHOSE ACTION RESULTS IN ENHANCED OSTEOCLASTIC ACTIVITY AND INCREASED OSSEOUS RESORPTION. THE UNDERSTANDING OF THE MODE OF ACTIVITY AND SITE OF ACTION OF OAF WILL GREATLY ENHANCE THE ABILITY TO CONTROL BONE LOSS ASSOCIATED WITH SUCH WOUNDS.							
30. APPROACH: (U) MONOCLONAL ANTIBODIES ARE RECOGNIZED FOR THEIR EXQUISITE SPECIFICITY IN THE ABILITY TO RECOGNIZE A SINGLE ANTIGENIC DETERMINANT. THIS TECHNOLOGY WILL BE UTILIZED TO DEVELOP A SYSTEM WHICH CAN BE USED TO EXTRACT PURE OAF FROM CULTURE SUPERNATANTS. SUCH MONOCLONAL ANTIBODIES COULD BE USED TO IDENTIFY THE PRESENCE OF OAF IN TISSUE SPECIMENS AND IDENTIFY THE ACTIVE SITE. BY REACTING OAF WITH MONOCLONAL ANTIBODIES IT CAN BE EXPECTED THAT OAF ACTIVITY COULD BE BLOCK IN VIVO. THIS PROJECT WAS STARTED UNDER DA088037.							
31. PROGRESS: (U) NONE.							

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				DA302827		01 OCT 83		REPORT CONTROL NUMBER VE9208	
1. DATE NEW UNIT		2. TYPE OF PROJECT		3. CURRENT STATE		4. WORK UNIT		5. WORK UNIT	
		A. NEW		U		U			
10. NO./CODES		PROGRAM ELEMENT		PROJECT NUMBER		TASK AREA NUMBER		WORK UNIT NUMBER	
		61102A		JMI811028510		DA		085	
11. CONTRIBUTION									
12. CONTRIBUTION									
13. TITLE (PROJECT AND WORK UNIT) (PROJECT AND WORK UNIT)									
(U) PRODUCTION AND UTILIZATION OF MONOCLONAL ANTIBODIES IN THE RAPID IDENTIFICATION OF ANAEROBIC MICROORGANISMS ASSOCIATED WITH MAXILLOFACIAL INFECTIONS									
14. SUBJECT TERMS AND GROUPS									
0803 BIODENGINEERING 0813 MICROBIOLOGY 0806 ENVIR BI									
15. TYPE (DAY)									
OCT 83									
16. CONT									
DA									
17. C. IN-HOUSE									
18. ESTIMATED ESTIMATE									
19. TOTAL YEARS									
1983 0.0									
1984 2.0									
20. PROFESSIONAL WORK YEARS									
21. FUNDS IN THOUSANDS									
\$ 0									
\$ 132									
22. NAME OF AWARD									
F. CUM/TOT: 0									
23. NAME OF ORGANIZATION									
MORDC INSTITUTE OF DENTAL RSCH USAID									
24. ADDRESS									
WASHINGTON DC 20307									
25. RESPONSIBLE PERSONAL									
NAME SWRENEY, T P									
TELEPHONE 202-878-3484									
26. CENTRAL OR									
MILITARY									
27. TITLE (PROJECT AND WORK UNIT) (PROJECT AND WORK UNIT)									
(U) MICROBIOLOGY; (U) WOUND INFECTIONS; (U) MONOCLONAL ANTIBODIES; (U) RAPID DETECTION; (U) LAB ANIMALS; (U) MICE; (U) RAM IV;									
28. OBJECTIVE: (U) MICROBIAL CONTAMINATION OF TRAUMATIC INJURIES TO THE MAXILLOFACIAL COMPLEX RESULTS IN DELAYED HEALING AND OTHER SEQUELAE WHICH HINDER RETURN OF THE PATIENT TO DUTY. A METHOD WHICH WILL RAPIDLY AND SPECIFICALLY IDENTIFY THE OFFENDING MICROORGANISMS WOULD BE MILITARILY RELEVANT IN ENHANCING WOUND HEALING IN MAXILLOFACIAL WAR WOUNDS. SUCH A SYSTEM COULD SERVE AS A USABLE MODEL IN THE RAPID DETECTION OF BIOLOGICAL WARFARE AGENTS.									
29. APPROACH: (U) THE REMARKABLE SPECIFICITY AND AVAILABILITY OF MONOCLONAL ANTIBODIES TO SELECTED MICROORGANISMS WILL BE UTILIZED TO DEVELOP A RAPID ASSAY SYSTEM ONCE THE ANTIBODIES CAN BE PRODUCED AND ISOLATED. THE SELECTION OF AN ASSAY SYSTEM WILL BE DEPENDENT ON SIMPLICITY, SPECIFICITY, SENSITIVITY, AND FIELD ADAPTABILITY. THIS PROJECT WAS STARTED UNDER DAOP8024.									
30. PROGRESS: (U) NONE.									

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				REPORT CONTROL SYMBOL	
DA0202228				01 OCT 83	
201708					
TO NO./CODES: A. NEW		U		U	
PROGRAM ELEMENT		PROJECT NUMBER		TASK AREA NUMBER	
01102A		3M181102B519		DA	
WORK UNIT NUMBER		089			
(U) A STUDY ON 80:80 PLA:PGA PLUS DIPHOSPHONISITIDE-LYSOZYME (DPI-L) FOR THE PROMOTION OF CALCIFICATION IN OSTEOUS DEFECTS					
002200 BIOCHEMISTRY 012800 PHYSIOLOGY					
OCT 83		CONT		DA	
C. IN-HOUSE					
F. CUM/TOT: 2 0					
038870		11		038870 11	
MORDC INSTITUTE OF DENTAL RECH USAIDR		MORDC INSTITUTE OF DENTAL RECH USAIDR		DA	
WASHINGTON DC 20307		WASHINGTON DC 20307			
SWEENEY, T P		MO 20		HOLLINGER, J O	
202-878-3484				202-878-3784	
F.I.C.A.					
MILITARY					
(U) LAB ANIMALS : (U) RATS : (U) DIPHOSPHONISITIDE-LYSOZYME : (U) BIOCOMPATIBLE : (U) BIODEGRADABLE : (U) IMPLANT : (U) BONE STIMULATING : (U) RAM IV:					
OBJECTIVE: (U) THE TECHNICAL OBJECTIVE WAS TO DETERMINE IF A BIODEGRADABLE, BIOCOMPATIBLE COPOLYMER OF POLYLACTIC ACID AND POLYGLYCOLIC ACID, IN COMBINATION WITH A DIPHOSPHONISITIDE INOSITOL-LYSOZYME COMPLEX, COULD INDUCE OSTEOGENESIS IN EXPERIMENTAL WOUNDS CREATED IN ENDOCHONDRAL AND INTRAMEMBRANOUS BONES. THE APPLICATIONS OF SUCH A MATERIAL WILL BE FOR FIXATION DEVICES AND AS IMPLANTS FOR OSSEOUS INDUCTION IN THE MAXILLOMANDIBULOFACIAL COMPLEX WHEN BONE IS LOST DUE TO TRAUMA, PATHOLOGY, OR ABLATION. BECAUSE APPROXIMATELY 10 PERCENT OF ALL COMBAT INJURIES ARE IN THE MALLIOMANDIBULOFACIAL REGION, DEVELOPMENT OF A BONE INDUCING AGENT IS HIGHLY IMPORTANT.					
APPROACH: (U) AFTER INSERTION OF THE IMPLANT MATERIALS, TISSUE COMPATIBILITY AND BONE INDUCTION TESTS WERE PERFORMED IN RABBITS AND RATS. SERUM AND HARD AND SOFT TISSUE PHOSPHATASES (ACID AND ALKALINE) WERE ASSAYED. HISTOMORPHOMETRY WAS PERFORMED ON PLASTIC EMBEDDED UNDECALCIFIED BONE, PROTEIN AND HYDROXYPROLINE ASSAYS WERE DONE, AND ATOMIC ABSORPTION SPECTROPHOTOMETRY WAS USED TO DETERMINE CALCIUM TO PHOSPHATE MOLAR RATIOS IN HOST BONE. ISOELECTRIC FOCUSING WAS ALSO FOR ISOENZYME IDENTIFICATION. THIS PROJECT WAS STARTED UNDER DA088037.					
PROGRESS: (U) NONE.					

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				DA302938		01 OCT 83		REPORT CONTROL SYMBOL 201708	
TO NO/CODES: A. NEW		U		U		NL		A. WORK UNIT	
PROGRAM ELEMENT		PROJECT NUMBER		TASK AREA NUMBER		WORK UNIT NUMBER			
01102A		3M1811028510		DA		870			
<p>FORMER ORJ BYOD: 82/83-0.2/8</p> <p>(U) IN VIVO EVALUATION OF ULYTRAMICROPOROUS CELLULOSE TRIACETATE WOUND DRESSINGS AS SLOW-RELEASE SYSTEM FOR ANTIBIOTICS</p>									
002800 BIOLOGY		003800 CLIN MEDICINE		010100 MICROBIO					
OCT 83		CONT		DA		C. IN-HOUSE			
DATE EFFECTIVE		EXPIRATION		FISCAL YEAR		FISCAL YEAR		FISCAL YEAR	
1983		1984		1983		1984		1985	
P. CUM/TOT: 8.9				0.0		0.0		0.0	
				0.0		0.0		0.0	
MORDC INSTITUTE OF DENTAL RECH USAIDR		WASHINGTON DC 20307		MORDC INSTITUTE OF DENTAL RECH USAIDR		WASHINGTON DC 20307			
RESPONSIBLE INDIVIDUAL		NAME		NAME		NAME		NAME	
SWEENEY, T P		MD 20		SETTERSTROM, J A		DA			
202-878-3484				202-878-3784					
P.I.C.A.				VINCENT, J W					
MILITARY									
<p>(U) LAB ANIMALS ; (U) GUINEA PIGS ; (U) RAM IV ; (U) WOUND DRESSING ; (U) SUSTAINED ANTIBIOTIC RELEASE</p>									
<p>OBJECTIVE: (U) UNTIL RECENTLY, AVAILABLE ARTIFICIAL WOUND DRESSINGS WERE MADE OF COTTON GAUZE. THESE DRESSINGS PROTECT WOUNDS FROM THE EXTERNAL ENVIRONMENT, BUT LITTLE ELSE. AN IMPROVED WOUND DRESSING THAT CLINGS TO WOUNDS WITHOUT ADHERING, KEEPS THE WOUND MOIST WITHOUT ALLOWING FLUID ACCUMULATION, ALLOWS OXYGEN EXCHANGE, AND PREVENTS INFECTION IS REQUIRED. IT IS THE OBJECTIVE OF THIS WORK TO DEVELOP A MATERIAL WITH THESE CHARACTERISTICS THAT IS EASILY APPLICABLE, WILL PROTECT THE WOUND, DECREASE INFECTION, AND ENHANCE WOUND HEALING.</p>									
<p>APPROACH: (U) AN ULYTRAMICROPOROUS CELLULOSE TRIACETATE MATERIAL (POROPLASTIC) WHICH POSSESSES MANY INHERENT CHARACTERISTICS THAT ARE THEORETICALLY DESIRABLE IN A WOUND DRESSING IS BEING EVALUATED IN VIVO. EFFORTS ARE DIRECTED TOWARD DEVELOPING THE MATERIAL AS A CONTROLLED RELEASE VEHICLE FOR ANTIBIOTICS. THIS PROJECT WAS STARTED UNDER DA008870.</p>									
<p>PROGRESS: (U) NONE.</p>									

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				PROJECT NUMBER		DATE OF REPORT		REPORT CONTROL SYMBOL	
				DA302838		01 OCT 82		Z01708	
1. DATE OF REPORT		2. NAME OF REPORT		3. NUMBER OF PAGES		4. DATE OF REVIEW		5. TYPE OF WORK UNIT	
		A. NEW		U		U		A WORK UNIT	
6. NO. OF COPIES		7. PROGRAM ELEMENT		8. PROJECT NUMBER		9. TASK AREA NUMBER		10. WORK UNIT NUMBER	
		81102A		3H1011028510		DA		801	
11. TITLE AND SUMMARY									
TITLE: ORU, STOD: 82/82-0.2/1									
SUMMARY: (U) BIOLOGICAL ACTIVITY VERIFICATION OF SPECIFIED MICROENCAPSULATED ANTIBIOTICS IN VIVO									
12. SUBJECT AND TECHNICAL AREA									
010100 MICROBIOLOGY			012800 PHARMACOLOGY			003800 CLIN MED			
13. START DATE		14. ESTIMATED COMPLETION DATE		15. FUNDING AGENCY		16. REPORTING METHOD			
OCT 82		CONT		DA		C. IN-HOUSE			
17. DISTRIBUTION		18. RESOURCES ESTIMATE		19. PROFESSIONAL MAN YRS		20. FUNDS IN THOUSANDS			
A. DATE EFFECTIVE		B. AMOUNT		C. YEAR		D. YEAR			
		F. CUM/TOT: \$ 0		1983		0.0		\$ 0	
		038870 11		1984		0.8		\$ 80	
21. INVESTMENT AND RELOCATION									
NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR					NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR				
ADDRESS: WASHINGTON DC 20307					ADDRESS: WASHINGTON DC 20307				
22. RESPONSIBLE INDIVIDUAL									
NAME: SWEENEY, T P					NAME: LETTERSTROM, J A				
TELEPHONE: 202-578-3484					TELEPHONE: 202-578-3784				
F.I.C.A. P.I.C.A.					SECURITY ACCOUNT NUMBER				
23. MULTIDISCIPLINARY APPLICATION					24. INVESTMENT AND RELOCATION				
MILITARY					DA				
25. EXTENDED SUMMARY (THIS SECTION IS OPTIONAL)									
(U) LAB ANIMALS ; (U) RATS ; (U) GUINEA PIGS ; (U) HAM IV (U) MICROENCAPSULATED ANTIBIOTICS ; (U) INFECTION CONTROL ; (U) SUSTAINED ANTIBIOTIC RELEASE									
<p>OBJECTIVE: (U) COMBAT WOUNDS ARE CHARACTERIZED BY HIGH INFECTION RATES DUE TO THE PRESENCE OF DEVITALIZED TISSUE AND FOREIGN BODIES CARRIED BY MISSILE FRAGMENTS. EVACUATION EXPOSES WOUNDS TO FURTHER CONTAMINATION AND DELAY BEFORE TREATMENT. IMPROVED METHODS TO DELIVER ANTIBIOTICS TO CONTAMINATED TISSUE FOLLOWING TRAUMATIC INJURY ARE NEEDED IN ORDER THAT SUSTAINED AND EFFECTIVE TISSUE LEVELS CAN BE MAINTAINED DESPITE REDUCED BLOOD PERFUSION FROM SHOCK OR DESTROYED BLOOD VESSELS. IT IS THE OBJECTIVE OF THIS WORK TO DEVELOP MICROSPHERES THAT SLOWLY RELEASE ANTIBIOTICS INTO CONTAMINATED WOUNDED TISSUE IN A THERAPEUTIC DOSE FOR AN EXTENDED TIME (14 DAYS). THE MICROSPHERES ARE APPLICABLE IN A SINGLE DOSE VIA AN AEROSOL SPRAY OR SHAKER-TYPE DISPENSER.</p> <p>APPROACH: (U) AMPICILLIN ANHYDRATE AND GENTAMICIN SULFATE ARE BEING INCORPORATED INDIVIDUALLY INTO MICROSPHERES OF BIOCOMPATIBLE, BIODEGRADABLE PLA:PGA COPOLYMER. THE MICROSPHERES ARE BEING ENGINEERED TO SLOWLY RELEASE THE ANTIBIOTIC OVER A KNOWN PERIOD, AFTER WHICH TIME THEY WILL COMPLETELY BIODEGRADE WITHIN THE WOUND SITE. THIS PROJECT WAS STARTED UNDER DA0A8021.</p> <p>PROGRESS: (U) NONE.</p>									

DD FORM 1488M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				PROJECT NUMBER		DATE OF REPORT		REPORT CONTROL SYMBOL	
1. DATE OF REPORT				0A202987		01 OCT 83		Z01708	
2. TYPE OF REPORT				U		U		NL	
3. NO. CODES				PROGRAM ELEMENT		PROJECT NUMBER		TASK AREA NUMBER	
4. NO. CODES				R1102A		2M1811028510		DA	
5. NO. CODES				FORMER		DA		803	
6. NO. CODES				MAX. OBJ. 8700		82/83-8.2/5			
7. TITLE				(U) A STUDY ON THE IMMUNOGENICITY OF THE COPOLYMER PLA:PGA USING A DOT ELISA METHOD					
8. NO. CODES				002300 BIOCHEMISTRY		012800 PHYSIOLOGY			
9. NO. CODES				DEC 83		CONT		G. IN-DOSE	
10. NO. CODES				F. CUM/TOT:		S. O			
11. NO. CODES				038670		11			
12. NO. CODES				MORDC INSTITUTE OF DENTAL RSCH USAIDR		MORDC INSTITUTE OF DENTAL RSCH USAIDR			
13. NO. CODES				WASHINGTON DC 20307		WASHINGTON DC 20307			
14. NO. CODES				SWEENEY, T P		HOLLINGER, J O		DA	
15. NO. CODES				202-878-3484		202-878-3764			
16. NO. CODES				F.I.C.A.					
17. NO. CODES				MILITARY					
18. NO. CODES				(U) LAB ANIMALS ; (U) RABBITS ; (U) RAM IV ; (U) KREBS CYCLE DERIVATIVES ; (U) IMMUNOLOGY ; (U) BIOPOLYMERS ; (U) DOT-ELISA					
<p>OBJECTIVE: (U) STUDIES HAVE DEMONSTRATED THAT BOTH MONOPOLYMERS AND COPOLYMERS OF CERTAIN KREBS CYCLE DERIVATIVES CAN BE EFFECTIVELY EMPLOYED AS WOUND REPAIR MATERIALS. THESE MATERIALS HAVE BEEN SHOWN TO BE TISSUE TOLERANT, BASED UPON CELLULAR EVALUATION. A RECENT ADVANCE IN THE FIELD OF IMMUNOLOGY HAS MADE IT POSSIBLE TO DETERMINE IF THE KREBS CYCLE BIOPOLYMERS ARE AS INNOCUOUS HUMORALLY AS THEY HAVE BEEN SHOWN TO BE CELLULARLY.</p> <p>APPROACH: (U) ANTISERUM REACTIVE WITH THE COPOLYMER PLA:PGA WILL BE PREPARED. THE COPOLYMER WILL ALSO BE PREPARED IN 1MG/NL AND 2MG/NL CONCENTRATIONS AND EMULSIFIED IN AN EQUAL VOLUME OF COMPLETE FREUND'S ADJUVANT. PLAIN COPOLYMER AND COPOLYMER PLUS ADJUVANT WILL SERVE AS THE IMMUNOGENS FOR IMMUNIZATION OF 2 EQUAL GROUPS OF RABBITS (5 ANIMALS/GROUP). THE DOT-ELISA METHOD WILL BE USED TO DETECT THE PRESENCE OF REACTIVE QUANTITIES (GREATER THAN NANOGRAM LEVELS) OF ANTIBODY IN THE RABBIT SERA RECOVERED AT WEEKLY INTERVALS FOR 8 WEEKS.</p> <p>PROGRESS: (U) NONE.</p>									

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				SECRET		DATE OF REPORT		REPORT CONTROL SYMBOL	
				DA305288		01 OCT 83		Z91704	
1. NEW UNIT		2. TYPE OF UNIT		3. CURRENT UNIT		4. WORK UNIT		5. WORK UNIT	
A. NEW		U		U		NL		A. WORK UNIT	
10. NO./CODES		PROGRAM ELEMENT		PROJECT NUMBER		TASK AREA NUMBER		WORK UNIT NUMBER	
81102A		3H181102B510		DA		802			
11. TITLE		12. DATE		13. DATE		14. DATE		15. DATE	
MUSE ORV. 8100		82/83-8.2/8							
(U) A STUDY TO EVALUATE A SYNTHETICALLY PRODUCED									
POLYPENTAPEPTIDE TO INDUCE OSTEOGENESIS									
002300 BIOCHEMISTRY 012800 PHYSIOLOGY									
16. START DATE		17. STOP DATE		18. START DATE		19. STOP DATE		20. START DATE	
OCT 83		CONT		DA		C. IN-HOUSE			
21. CONTRACT NUMBER		22. CONTRACT NUMBER		23. CONTRACT NUMBER		24. CONTRACT NUMBER		25. CONTRACT NUMBER	
26. DATES OF INTERVIEW		27. DATES OF INTERVIEW		28. DATES OF INTERVIEW		29. DATES OF INTERVIEW		30. DATES OF INTERVIEW	
31. TYPE		32. TYPE		33. TYPE		34. TYPE		35. TYPE	
F. CUM/TOT.		S. O							
36. INVESTIGATOR		37. INVESTIGATOR		38. INVESTIGATOR		39. INVESTIGATOR		40. INVESTIGATOR	
038870		11		038870		11			
MORDC INSTITUTE OF DENTAL RSCH USAIDR					MORDC INSTITUTE OF DENTAL RSCH USAIDR				
WASHINGTON DC 20307					WASHINGTON DC 20307				
RESPONSIBLE INDIVIDUAL					RESPONSIBLE INDIVIDUAL				
NAME SWEENEY, T P					NAME HOLLINGER, J O				
TELEPHONE 202-678-3484					TELEPHONE 202-678-3784				
11. DATES OF INTERVIEW					11. DATES OF INTERVIEW				
F.I.C.A.					F.I.C.A.				
11. DATES OF INTERVIEW					11. DATES OF INTERVIEW				
MILITARY					MILITARY				
(U) LAB ANIMALS ; (U) RATS ; (U) RAM IV ; (U) IMPLANT ; (U)									
CRANIO-MANDIBULOFACIAL COMPLEX ; (U) POLYPENTAPEPTIDE ; (U) NEW BONE FORMATION									
OBJECTIVE: (U) NUMEROUS INVESTIGATIONS HAVE BEEN CONDUCTED USING A VARIETY OF IMPLANT MATERIALS TO SUPPORT AND TO PROMOTE OSSEOUS WOUND REPAIR OF THE CRANIO-MANDIBULOFACIAL COMPLEX. THE PURPOSE OF THE PROPOSED INVESTIGATION IS TO DETERMINE IF A SYNTHETICALLY DERIVED POLYPENTAPEPTIDE CAN INDUCE NEW BONE FORMATION IN ENDOCHONDRAL WOUNDS IN THE DIAPHYSES OF THE TIBIAS OF RATS.									
APPROACH: (U) THE AREA OVERLYING THE ANTERIO MEDIAL ASPECTS OF THE RIGHT TIBIAS OF 70 ADULT WALTER REED RATS WILL BE PREPARED FOR INSERTION OF A POLYPENTAPEPTIDE IMPLANT. THE LEFT DIAPHYSEAL AREA WILL SERVE AS A CONTROL. AT 3, 7, 14, 21, 28, AND 42 DAY INTERVALS TEN ANIMALS WILL BE EUTHANIZED AND BONE HOST-IMPLANT AND CONTROL SITES WILL BE RECOVERED AND TISSUES WILL BE PROCESSED FOR PLASTIC EMBEDDING, HISTOCHEMISTRY, AND HISTOMORPHOMETRY. THE HETEROTOPIC SITES FOR POLYPENTAPEPTIDE EVALUATION WILL BE THE RIGHT GLUTEAL MUSCLE MASS. AFTER INSERTION OF THE IMPLANT, SPECIMENS WILL BE RECOVERED AT 7, 21, AND 42 DAYS AND WILL BE PROCESSED FOR HISTOLOGIC EXAMINATION.									
PROGRESS: (U) NONE.									

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION ^a	2. DATE OF SUMMARY ^a	REPORT CONTROL SYMBOL DD-DRAE(AR)036	
3. DATE PREP SUBMIT ^a	4. KIND OF SUMMARY	5. SUMMARY SCTY ^a	6. WORK SECURITY ^a	7. STORAGE ^a	8. DISSEM INSTR ^a	9. SPECIFIC DATA CONTRACTOR ACCESS	10. LEVEL OF SUM A. WORK UNIT
821001	H. TERM	U	U		NL	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	
11. NO./CODES ^a	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER		WORK UNIT NUMBER	
a. PRIMARY	62775A	3S162775A825		AR		014	
b. CONTINUING							
c. CONTINUING		STOG 82/82-6.2:4					
12. TITLE (Provide with Security Classification Code) ^a							
(U) Preventive Dentistry Measures of Military Significance							
13. SCIENTIFIC AND TECHNOLOGICAL AREAS ^a							
012900 Physiology		002400 Bioengineering		003500 Clinical Medicine			
14. ENTRY DATE		15. ESTIMATES COMPLETION DATE		16. FUNDING AGENCY		17. PERFORMANCE METHOD	
7101		CONT		DA		C. IN-HOUSE	
18. CONTRACT/GRANT				19. RESOURCES ESTIMATE		20. PROFESSIONAL MAN YRS	
a. DATES/EFFECTIVE:				b. PRESENTING		c. FUNDS (in thousands)	
b. NUMBER ^a				FISCAL YEAR		83	
c. TYPE:				FUNDING YEAR		0.2	
d. KIND OF AWARD:						50	
e. AMOUNT:							
f. CUM. AMT.							
21. RESPONSIBLE SCS ORGANIZATION				22. PERFORMING ORGANIZATION			
NAME ^a U.S. Army Institute of Dental Research				NAME ^a U.S. Army Institute of Dental Research			
ADDRESS ^a Washington, DC 20307				ADDRESS ^a Washington, DC 20307			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Provide SSAN if U.S. Academic Institution)			
NAME: SWEENEY, T. P.				NAME ^a LORTON, L.			
TELEPHONE: (202) 576-3484				TELEPHONE: (415) 561-4845			
				SOCIAL SECURITY ACCOUNT NUMBER: POC:DA			
23. GENERAL USE				ASSOCIATE INVESTIGATORS			
Foreign Intelligence Considered				NAME: MADER, C.			
				NAME: GROVER, P.			
24. REVISIONS (Provide each with Security Classification Code)							
(U) Marginal Leakage; (U) Resin Restorative;							
(U) Post and Core Restorations; (U) Dental Emergencies							
25. TECHNICAL OBJECTIVE, 26. APPROACH, 27. PROGRAM (Provide individual paragraphs identified by number. Provide text of each with Security Classification Code.)							
<p>23. (U) To develop new and simplified methods of preventing disease related dental emergencies in the field. To assess new methods of (1) improving the biologic management of militarily relevant oral conditions and (2) improving the cost-effectiveness factors of preventive dental therapy in the military.</p> <p>24. (U) Studies will be conducted which will (1) develop and evaluate improved methods of dental care which will prevent dental emergencies in the field; (2) develop more rapid and effective means of identifying and treating soldiers with at-risk-profiles for field dental emergencies.</p> <p>25. (U) (8210-8310) Records of emergency and routine visits to two of three dental clinics are being collected in order to determine factors in dental status that contribute to emergency visits. The data gathering phase is 75% complete. All data collection will be completed by 15 November. Final analysis of the data will begin as soon as the data base can be compiled. Study of a simplified method for restoring endodontically treated teeth using composite resins has appeared to be promising as a field expedient, but was terminated due to personnel losses.</p>							

^a Available to contractors upon originator's approval

DD FORM 1498

PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. DD FORMS 1498, 1 MAY 67, AND 1498-1, 1 MAR 68 (FOR ARMY USE) ARE OBSOLETE.

PROJECT: 3S16277A825

WORK UNIT TITLE: (U) Preventive Dentistry Measures of Military Significance

PRINCIPAL
INVESTIGATOR: LTC Lewis Lorton, DC

Evaluation of a New Restorative Procedure for Resin Restorations
Designed to Prevent Dental Emergencies on the Battlefield

Problem: Marginal leakage, at the tooth/restoration interface, is a weakness shared by all restorations done with traditional restorative materials and operative techniques. Marginal leakage of restorations may cause or contribute to several undesirable consequences to include: recurrent caries, staining, postoperative pain, chronic hypersensitivity, and pulpal pathosis. Any one, or combination of these conditions, may lead to premature failure of the restoration and/or the production of a dental emergency on the battlefield, necessitating removal of the soldier from combat. The development of techniques to decrease or eliminate marginal leakage around restorations is thus highly desirable.

Approach: Extracted human teeth will be used in the study. Cavity preparations with traditional and experimental cavosurface margin designs will be prepared. The cavity preparations will be restored with several commercial dental resins and the teeth dissolved with nitric acid. The remaining resin restorations will be prepared for scanning electron microscopic evaluation. The scanning electron microscope will be used to evaluate the adaptation of the various resins to the traditional and experimental cavity designs. If the adaptation is good, then leakage studies will be done followed by clinical testing.

Results: It was determined from scanning electron microscopic evaluation that all of the commercial dental resins adapted well to both the traditional and experimental cavosurface margin designs. Tooth harvest, literature review, and discussions are currently taking place so that the leakage studies can be done as the next planned step.

PROJECT: 38162775/825

WORK UNIT TITLE: (U) Preventive Dentistry Measures of Military Significance

PRINCIPAL
INVESTIGATOR: COL Carmon L. Mader, DC

Evaluation of a New Restorative Procedure for Post and Core Restorations Designed to be More Economical and to Prevent Dental Emergencies on the Battlefield

PROBLEM: Post and core restorations are involved in the restoration of teeth that have been endodontically treated. The traditional techniques used to fabricate post and core restorations are very time consuming and expensive as these techniques require substantial amounts of time from the doctor, the dental assistant, the laboratory technician, and the patient. In addition, relatively large amounts of precious metals (usually gold) are required. Also, the exacting various steps to be redone. In addition, trauma to anterior teeth that have been treated with traditional cast metal post and core restorations frequently results in a fracture of the root and subsequent loss of the tooth. These teeth must then be replaced requiring additional time (by the dentist, dental assistant, dental laboratory, and patient) and expense (precious metal framework for a fixed or removable prosthesis). The development of new, simplified, more economical techniques for post and core fabrication, that require less personnel time and do not utilize precious metals, is highly desirable. Composite resins adapt well to etched tooth surfaces and have reasonable compression strength. This material may be satisfactory for use in new, simplified, more economical techniques for post and core fabrication.

APPROACH: Extracted, single-rooted, human teeth will be used in the research. Routine endodontic therapy will be performed in their canals. The canals will then be etched with acid to remove the smeared layer produced by instrumentation. Next, the canals will be filled with a low viscosity resin. The teeth will be longitudinally split in half and processed for scanning electron microscopic evaluation. The scanning electron microscope will be used to evaluate how well the resin adapted to the dentinal tubules. If the resin adaption is good, then additional studies will be done to evaluate leakage and shear strength. If these studies are promising, then clinical testing of the technique is planned.

RESULTS: It was determined from scanning electron microscopic evaluation that the low viscosity resin reliably penetrated the dentinal tubules and adapted well to them. Tooth harvest, literature review and discussions are currently taking place so that the leakage and shear strength studies can be done as the next planned step.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				PROJECT NUMBER		DATE OF REPORT		REPORT CONTROL NUMBER	
				DA008022		01 OCT 83		VEJ05A	
1. DATE OF ENTRY		2. TYPE OF ENTRY		3. ENTRY BY		4. WORK SECURITY		5. ENTRY BY	
01 OCT 83		D. CHANGE		U		U		CX	
6. NO. CODES		7. PROGRAM ELEMENT		8. PROJECT NUMBER		9. TASK AREA NUMBER		10. WORK UNIT NUMBER	
82778A		35102778A021		AS		002			
11. CONTINUED		12. CONTINUED		13. CONTINUED		14. CONTINUED		15. CONTINUED	
(U) DEVELOPMENT AND EVALUATION OF DENTAL MATERIALS AND MATERIEL FOR ARMY USE.									
16. SUBJECT AREA OR SUBJECT									
1107 MISC MAT 0704 PHYS CHEM 0702 INORG CH									
17. START DATE									
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18. CONTINUED									
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19. CONTINUED									
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20. RESEARCH ORGANIZATION									
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(U) STORAGE STABILITY ; (U) COMPOSITE RESTORATIVES ; (U) IMPRESSION MATERIALS ; (U) CORROSION OF ALLOYS ; (U) PORCELAIN-METAL BOND ; (U) RAM IV

OBJECTIVE: (U) TO EVALUATE NEW MATERIALS AND MATERIEL OF SPECIAL INTEREST TO THE ARMY DENTIST. CRITERIA FOR SELECTION OF MATERIALS, DEVICES OR TECHNIQUES FOR EVALUATION ARE BASED ON ANTICIPATED HIGH POTENTIALS FOR- (1) SAVINGS OF FISCAL AND/OR MANPOWER RESOURCES- (2) WORK SIMPLIFICATION- (3) IMPROVED HEALTH CARE DELIVERY IN COMBAT AREAS- AND (4) ENHANCED SAFETY WITH RESPECT TO PROFESSIONAL AND ANCILLARY PERSONNEL AS WELL AS TO THE PATIENT.

APPROACH: (U) NEW MATERIALS WILL BE EVALUATED ON THE BASIS OF THE FOLLOWING PARAMETERS- COMPOSITION, MICROSTRUCTURE, PHYSICAL AND MECHANICAL PROPERTIES, CYTOTOXICITY, AND CLINICAL PERFORMANCE. STORAGE STABILITY OF MATERIALS FOR FIELD USE WILL BE EVALUATED.

PROGRESS: (U) THE INTERACTION BETWEEN OPAQUE LIQUIDS AND CERAMIC METALS HAS BEEN DEMONSTRATED. VITA LIQUID DEMONSTRATED THE LOWEST CONTACT ANGLES FOLLOWED BY NEY, CERAMIC, VILL-CREAM, AND BIO BOND LIQUIDS. SURFACE ROUGHNESS PREPARATION WAS FOUND TO HAVE STATISTICALLY SIGNIFICANT EFFECTS ON CONTACT ANGLE MEASUREMENTS ON OPTION, BAKE-ON N/P, AND TRIUMPH METALS. SITE VISITS TO THE SIXTH U.S. ARMY LOGISTICS COMMAND AND LETTERMAN ARMY MEDICAL CENTER LOGISTICS DIVISION PROVIDED SUFFICIENT DATA ON WHICH TO BASE RECOMMENDATIONS FOR THE DELETION OF GROUPS OF SUPPLIES FROM CONSIDERATION FOR STORAGE STABILITY EVALUATION INASMUCH AS THEY ARE NOT PROJECTED FOR FIELD USE. ADDITIONAL WORK DONE UNDER AGENCY ACCESSION NUMBER DA302899 AND DA302904.

PROJECT: 38162775A825

WORK UNIT TITLE: (U) Development and Evaluation of Dental Materials
and Materiel for Army Use

PRINCIPAL
INVESTIGATOR: LTC G. D. Woplsy, DC

Surface Phenomenon of Opaque Porcelain on

Oxidized Metal

PROBLEM: The ease of manipulation of porcelain and metal systems is of paramount importance in the modern military dental laboratory. Knowledge of handling characteristics of porcelain opaque suspensions on oxidized metal surfaces can improve the fabrication time of restorations and benefit the military dental laboratory in training and utilizing constantly rotating personnel.

APPROACH: The wetting mediums for five dental opaque porcelains were evaluated by sessile drop contact angle measurements technique on five dental ceramic alloys. Eight replications on both smooth and sand-blasted metal surfaces were evaluated in a fully randomized design.

RESULTS: Statistically significant interactions of opaque liquids on specific ceramic metals were observed in this study, indicating that broad generalizations of the wetting characteristics of opaque liquids on oxidized metals cannot be made. Even though a trend did develop with Vita liquid demonstrating the lowest contact angles, followed by Ney, Ceramco, Will-Ceram, and Biobond; the statistical significance of this ranking varied with each of the five metals and two surfaces evaluated. Surface roughness preparation was found to have statistically significant effects on contact angle measurements on Option, Bake-on N/P, and Triumph metals.

PROJECT: 38162775A825

WORK UNIT TITLE: (U) Development and Evaluation of Dental Materials and Materiel for Army Use

PRINCIPAL INVESTIGATOR: LTC G. D. Woolsey, DC

Storage Stability of Medical and Dental Materiel

PROBLEM: Dental and medical materiel currently used by the U.S. Army Medical Department is stored in 6 major depots (2-in CONUS, 2-in Asia, and 2-in Europe). The monitoring of the serviceability of these supplies is outlined in "Appendix M" of the "Quality Control Depot Serviceability Standards". The standards outlined in "Appendix M" are those derived from manufacturers and are usually tests of no more than 60°C for one week. Dental and Medical teams must be able to depend upon supplies which will function after prolonged storage in areas of varying temperature and humidity.

APPROACH: The initial phase of this work will be the collection of background information on the Army medical supply storage system, how materials and supplies are stored, types of materiel stored and the storage environments within the major medical supply depots. The basis of this investigation will be information within AR 40-61, site visits to Tracy Army Depot, the Defense Procurement Support Command (where some limited materials testing is conducted on materials in the Army supply system), and the U.S. Army Medical Materiel Agency (source of world-wide deployment of medical and dental supplies). The second phase of this study will be the laboratory testing of those dental and medical supplies found in medical depots and determined potentially sensitive to adverse environmental storage conditions. It is imperative that the temperature and humidity within each major storage facility be determined to properly design a laboratory study of storage stability. Knowledge of perishable supplies currently stored in the major depots (as outlined in Appendix "E" of AR 40-61) will yield a study design more relevant to the modern mobile Army. An environmental chamber model LR-386-C-MP will be used to evaluate environmental effects on dental and medical materiel.

RESULTS: The identification of major military depots where major and minor medical assemblages are stored has been accomplished through site visits to the Sixth U.S. Army Logistics Command and the Letterman Army Medical Center Logistics Division. The evaluation of "Appendix M" of "Quality Control Depot Serviceability Standards" and AR 40-61 have formed the reference basis for the initial work on this project. Through the initial phase of this work, groups of materials have been identified which are not stored and can be deleted from consideration for this study.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACRONYM	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL	
				DA OG 6034	83 10 01	DD-DRAE(AR)336	
3. DATE PREVIOUS SUMMARY	4. TYPE OF SUMMARY	5. SUMMARY CATEGORY	6. WORK SECURITY	7. PROGRAM	8. WORK NUMBER	9. SPECIFIC DATA: CONTRACTOR ACCESS	10. LEVEL OF SUMMARY
82 10 01	H. TERM	U	U		NL	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	A. WORK UNIT
11. NO./CODES	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER			
a. PRIMARY	62775A	3S162775A825	AB	003			
b. CONTRIBUTING	62775A	3S162775A825	AC	003			
c. WORK UNIT NUMBER: STOG: 80-7.2.5							
12. TITLE (Provide title and security classification code)							
(U) Development and Improvement of Metallic Restorative Materials							
13. SCIENTIFIC AND TECHNOLOGICAL AREA							
009900 Metallurgy and Metallography; 008300 Inorganic Chemistry; 002400 Bioengineering							
14. START DATE	15. ESTIMATED COMPLETION DATE	16. FUNDING AGENCY	17. PERFORMANCE METHOD				
69 01	CONT	DA	C. IN-HOUSE				
18. FUNDING AGENCY			19. RESOURCES ESTIMATE	20. PROFESSIONAL MAN YRS		21. FUNDS (in thousands)	
a. DATES/EFFECTIVE:			PREESTIMATE				
b. NUMBER:			FISCAL YEAR	83		0.3	
c. TYPE:			CURRENT YEAR	84		0	
d. KIND OF AWARD:			F. CUM. AMT.		0		
22. RESPONDING DOD ORGANIZATION			23. PERFORMING ORGANIZATION				
NAME: U.S. Army Institute of Dental Research			NAME: U.S. Army Institute of Dental Research				
ADDRESS: Washington, DC 20307			ADDRESS: Washington, DC 20307				
RESPONSIBLE INDIVIDUAL			PRINCIPAL INVESTIGATOR (Provide SSAN if U.S. Academic Institution)				
NAME: SWEENEY, T.P.			NAME: VERMILYEA, S.				
TELEPHONE: (202) 576-3484			TELEPHONE: (415) 752-8343				
			SOCIAL SECURITY ACCOUNT NUMBER: POC:DA				
24. GENERAL USE:			ASSOCIATE INVESTIGATORS				
			NAME: WOOLSEY, G.				
			NAME:				
25. REVISIONS (Provide date and reason for revision)							
(U) Base Metal Alloys; (U) Casting Accuracy;							
(U) Soldering Base Metals; (U) Investment Techniques							
26. TECHNICAL OBJECTIVE, 27. APPROACH, 28. PROGRAM (Provide individual paragraphs identified by number. Precede text of each with Security Classification Code.)							
<p>23. (U) Annual Army expenditures for precious metals utilized in the fabrication of fixed dental prostheses are in the vicinity of \$1,000,000. The cost of an equal volume of base metal alloy is \$30,000. Properties of base metal alloys indicate however, that these alloys cannot be utilized for small castings without drastic metallurgical modifications. This work is therefore being conducted to (1) develop heat treatment methods for controlling properties of nickel-chromium based casting alloys; (2) evaluate nickel-chromium based alloys for use in operative dentistry.</p> <p>24. (U) The properties of nickel-chromium based alloys will be studied in detail by various physical methods available in order to devise procedures which will optimize their usefulness. Any improvement obtained will be evaluated clinically.</p> <p>25. (U) Loss of the principal investigator prevented significant progress on this work unit. Continued efforts to develop reliable techniques for soldering base metal alloys have not been successful.</p>							

* Available for reproduction upon originator's approval

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL	
				DA 066679	831001	DD-DR&E(AR)636	
3. DATE PREP SUMMARY	4. KIND OF SUMMARY	5. SUMMARY ACT	6. WORK SECURITY	7. REGRADING	8. DISSEM INSTR	9. SPECIFIC DATA - CONTRACTOR ACCESS	10. LEVEL OF SUM
821001	H. TERM	U	U		NI	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	A. WORK UNIT
11. NO./CODES	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER		WORK UNIT NUMBER	
	62775A	3S162775A825		AB		010	
12. CONTRIBUTING							
A. CONTRIBUTING							
B. CONTRIBUTING		STOG 80-7.2:5					
13. TITLE (Provide only security classification code)							
(U) The Initial Treatment of Combat Wounds							
14. SCIENTIFIC AND TECHNOLOGICAL AREA							
012600 Pharmacology		012900 Physiology		002300 Biochemistry			
15. START DATE		16. ESTIMATED COMPLETION DATE		17. FUNDING AGENCY		18. PERFORMANCE METHOD	
8101		CONT		DA		C. IN-HOUSE	
19. SUMMARY/STATUS				20. RESOURCES ESTIMATE		21. PROFESSIONAL MAN YRS	
A. DATE/EFFECTIVE:				B. FISCAL YEAR		C. FUNDS (in thousands)	
B. NUMBER:				83		1.0	
C. TYPE:				SUMMARY		99	
D. KIND OF AWARD				E. CUM. AMT.			
22. RESPONSIBLE ORG ORGANIZATION				23. PERFORMING ORGANIZATION			
NAME: U S Army Institute of Dental Research				NAME: U S Army Institute of Dental Research			
ADDRESS: Washington, DC 20307				ADDRESS: Washington, DC 20307			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Provide NAME if U.S. Academic Institution)			
NAME: SWEENEY, T. P.				NAME: SETTERSTROM, J. A.			
TELEPHONE: (202) 576-3484				TELEPHONE: (202) 576-2290/3662			
				SOCIAL SECURITY ACCOUNT NUMBER: POC:DA			
24. GENERAL USE				25. ASSOCIATE INVESTIGATORS			
Foreign Intelligence Considered				NAME: VINCENT, J.			
				NAME:			
26. REVENUE (Provide NAME and NUMBER Description Code)							
(U) Cellulose Triacetate; (U) Gentamicin; (U) Copolymer Bandage; (U) Lidocaine; (U) Laboratory Animals							
27. TECHNICAL OBJECTIVE, 28. APPROACH, 29. PROGRESS (Provide individual paragraphs identified by number. Provide last of each with security classification code.)							
<p>23. (U) To develop a multipurpose wound dressing which will provide anesthesia, antisepsis and hemostasis so that, where appropriate, the result will be rapid return of the wounded soldier to duty as well as reduction of the morbidity occasioned by delayed definitive treatment and secondary complications.</p> <p>24. (U) Contract developed drug release systems will be evaluated in animal models developed specifically for that purpose. Various methods and materials for maintaining contact over a variety of maxillofacial contours will be evaluated for their utility of application and use in the combat situation.</p> <p>25. (U) 8209-8309 Wounds infected with <u>Staphylococcus aureus</u> ($> 10^5$ organisms/cm²) when covered with POROPLASTIC[®] impregnated with gentamicin (6.0 - 8.0% w/w) were freed of infection. The POROPLASTIC[®] appears to provide an excellent vehicle for sustained topical delivery of antibiotics and shows promise as an improved wound dressing. In future studies additional antibiotics will be incorporated and efforts will be directed toward improving its ability to cling to the wound surface.</p>							

* Available to contractors upon originator's approval.

DD FORM 1498

PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. DD FORMS 1498A 1 NOV 68 AND 1498 1 MAR 69 (FOR ARMY USE) ARE OBSOLETE.

PROJECT: 3S162775A825

WORK UNIT TITLE: (U) The Initial Treatment of Combat Wounds

PRINCIPAL
INVESTIGATOR: Jean A. Satterstrom, Ph.D.

In Vivo Evaluation of POROPLASTIC® Wound Dressings

Problem: Until recently, available artificial wound dressings were made of cotton gauze. These dressings are unable to prevent wound surface dehydration and due to wound adherence, they are difficult to remove without disrupting the healing process. Research has confirmed that epithelialization proceeds most rapidly in a moist environment. Easily applied wound dressings are needed which will provide a moist environment, are permeable to oxygen, resist bacterial permeation, are bactericidal, and promote wound healing.

Approach: POROPLASTIC® a material made of cellulose triacetate, is available for development of a new wound dressing. It is ultramicro-porous and easily impregnated with drugs which release slowly into aqueous solutions. The material is supple, resilient, conformable to wound topography, and transparent, which allows for continuous observation of wounds. Moisture vapor transmission, oxygen permeability, biocompatibility, and toxicity tests must be performed to evaluate its applicability as an optimal wound dressing. Its ability to release drugs into tissue has been investigated. Gentamicin-impregnated POROPLASTIC® has been overlaid on wound infected with gentamicin-sensitive Staphylococcus aureus. Wash solutions obtained by repeated scrubbing of the wound surface were subjected to bacterial plate counts to ascertain the quantity of viable bacteria/cm². The bacterial counts obtained for treated and untreated wounds were compared.

Results: A comparison was made of the effectiveness of cellulose triacetate wound dressings which were either unloaded or loaded with gentamicin (4.0-6.4 wt%). All wound dressings had been applied to animal wounds infected with 4.5×10^6 cfu of S. aureus. After three days, all control wounds yielded an average of 5.59×10^7 S. aureus, while the gentamicin-treated group yielded an average of 7.21×10^7 . Those animals that had received a wound dressing of ≥ 6 wt% gentamicin (n=4) had sterile wounds. When wound dressings were placed on freshly reinfected, established wounds, control animals displayed 3.76×10^7 S. aureus while the gentamicin-treated group (≥ 6.2 wt%) yielded an average of 8.6×10^7 S. aureus. Results to date indicate the the POROPLASTIC® impregnated with ≥ 6 wt% gentamicin provides an effective means of treatment for both acute and established infections of S. aureus.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACRONYM ^a	2. DATE OF SUMMARY ^a	REPORT CONTROL SYMBOL DD-DR&E(AR)636	
3. DATE PREV SUMMARY	4. KIND OF SUMMARY	5. SUMMARY ICY ^a	6. WORK SECURITY ^a	7. ACRONYM ^a	8. COUNCIL INSTR ^a	9. SPECIFIC DATA CONTRACTOR ACCESS	10. LEVEL OF SUM A. WORK UNIT
821001	H. TERM	U	U	DA OG 8670	NL	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	
11. NO./CODES ^a	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER			
A. PRIMARY	62775A	3S162775A825	AB	013			
B. CONTRIBUTING							
C. CONTRIBUTING	/ / / / / / / / STOG 82/83-6.2/4						
11. TITLE (Provide with security classification code) ^a							
(U) Development and Evaluation of Dental Material for Field Use							
12. SCIENTIFIC AND TECHNOLOGICAL AREA ^a							
002400 Bioengineering; 010300 Miscellaneous Materials; 008500 Isotopes							
13. START DATE		14. ESTIMATED COMPLETION DATE		15. FUNDING AGENCY		16. PERFORMANCE METHOD	
8110		CONT		DA		C. IN-HOUSE	
17. CONTRACT/GRANT				18. PERSONNEL ESTIMATE		19. PROFESSIONAL MAN YRS	
A. DATES/EFFECTIVE:				B. PREVIOUS		C. FUNDS (in thousands)	
B. NUMBER:				FISCAL YEAR		2.0	
C. TYPE:				4. AMOUNT:		165	
D. KIND OF AWARD:				F. SUM. AMT.			
20. RESPONSIBLE DSO ORGANIZATION				21. PERFORMING ORGANIZATION			
NAME: U.S. Army Institute of Dental Research				NAME: U. S. Army Institute of Dental Research			
ADDRESS: Washington, DC 20307				ADDRESS: Washington, DC 20307			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Provide SSAN if U.S. Academic Institution)			
NAME: SWEENEY, T.P.				NAME: VANDRE, R.			
TELEPHONE: (202) 576-3484				TELEPHONE: (415) 561-3162			
				SOCIAL SECURITY ACCOUNT NUMBER: POC:DA			
22. GENERAL USE				ASSOCIATE INVESTIGATORS			
Foreign Intelligence Considered				NAME: LORTON, L.			
				NAME: GROVER, P.			
23. (U) Dental X-ray; (U) Dental Cutting Instrument; (U) Subtraction Radiography; (U) Radionuclide X-ray System; (U) Laboratory Animals							
24. (U) To assist in the development of dental equipment capable of reliable performance and easy maintenance under all field operational conditions. Included are the development of concepts for field dental equipment which is miniaturized, light-weight, energy efficient and low cost.							
25. (U) Conceptual and basic engineering requirements for a field dental x-ray system and a field dental cutting instrument will be studied. Current technology will be reviewed for its ability to produce the needed design criteria and advanced technology requirements will be identified. Experimental devices will be constructed.							
26. (U) A prototype dental x-ray camera has been designed and fabricated which is the size of a pack of cigarettes, weighs eight ounces, requires no electrical power, and is nearly indestructible. This unit uses radioactive Gadolinium as its x-ray source with a half-life of nearly one year. Equipment allowing standardization of radiographs has been developed and a comparison between conventionally viewed and computer subtraction processes radiographs has been completed. Diagnostic accuracy is greatly enhanced using computer subtraction techniques. Very small changes in bone apposition following arrest of disease were successfully documented in the monkey, but histologic correlation has not been completed. No results are yet available from the implant studies.							

^a Available to contractors upon written request.

DD FORM 1498

PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. (1) 1 MAR 66 (FOR ARMY USE) ANY OBSOLETE

PROJECT: 3S162775AB25

WORK UNIT TITLE: (U) Development and Evaluation of Dental Material
for Field Use

PRINCIPAL
INVESTIGATOR: MAJ Robert H. Vandre, DC

Design and Evaluation of a Combat Field X-Ray Unit

Using a Radiographic Source

PROBLEM: The present dental X-ray unit is a cumbersome, relatively delicate instrument. It is nothing more than an office X-ray unit that fits into a carrying case. It requires two men to transport it and needs 100 volts AC to power it. This unit also requires a darkroom and processing equipment which also tend to reduce the portability of the system.

APPROACH: In concert with the Dental Radiology Department, University of California at San Francisco, an extremely portable dental X-ray unit is being developed which will use a radioactive source to generate x-rays. The use of Polaroid® film with image-intensifying screens is being explored to remove the need for a darkroom and developer.

RESULTS: A contract for the joint development and testing of the above system was drawn with the Dental Radiology Department, University of California at San Francisco. A prototype dental X-ray camera has been designed and fabricated. It is the size of a pack of cigarettes, weighs eight ounces, requires no electrical power, and is nearly indestructible. This unit uses radioactive Gadolinium as its x-ray source with a half-life of nearly one year. Preliminary data shows that x-ray exposure levels to the patient will be 200 times less than those taken with conventional dental X-ray units. Radiographs of the skull taken using this system show details with clarity at least as good as conventional Panorex radiographs.

PROJECT: 3S162775A825

WORK UNIT TITLE: (U) Development and Evaluation of Dental Material
for Field Use

PRINCIPAL
INVESTIGATOR: MAJ Michael P. Rethman, DC

Subtraction Radiography for the Diagnosis of
Bone Lesions in Dogs

PROBLEM: A computer program has been developed at NIH to allow processing of sequential standardized radiographs by digital computer. Structured noise (unchanged imagery) is eliminated by subtraction, leaving only images of that which has changed. Such radiographs would be extremely useful for monitoring osseous healing in experimental animals if correlation could be made with demonstrated histological and established wound healing parameters. Equipment allowing standardization of radiographs in a live animal model was to be developed. Following development of such equipment, the usefulness of computer subtracted images for location of osseous wounds was to be determined. If preliminary data was promising, documentation of osseous wound healing was to be evaluated.

APPROACH: Radiographic cones were manufactured which keyed directly into custom splints which held the film in a reproducible relationship. Small intraosseous wounds were placed in the mandibles of anesthetized dogs and sequential healing radiographs were secured. One monkey which had naturally progressive periodontal disease was documented following nonsurgical treatment designed to arrest that disease. Current implant studies were documented using the same radiographic equipment.

RESULTS: The equipment allowing standardization of radiographs has been developed and a comparison between conventionally viewed and computer subtraction processed radiographs has been completed. Diagnostic accuracy is greatly enhanced using computer subtraction techniques. Very small changes in bone apposition following arrest of disease were successfully documented in the monkey, but histologic correlation has not been completed. No results are yet available from the implant studies.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. REPORT NUMBER	2. DATE OF REPORT	REPORT CONTROL SYMBOL	
				DA OG 8672	83 10 01	DD-382B(AR)326	
3. DATE PREPARED	4. KIND OF SUMMARY	5. SUMMARY CITY	6. WORK SECURITY	7. RESEARCH	8. SOURCE STATE	9. SPECIFIC DATA CONTRACTOR ACCESS	10. LEVEL OF USE
82 10 01	H. TERM	U	U		NL	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	A. WORK UNIT
11. NO. / CODE	PROGRAM ELEMENT	PROJECT NUMBER		TASK AREA NUMBER		WORK UNIT NUMBER	
6	62775A	3S162775A825		AB		019	
12. DOWNGRADING							
13. STOG 82/83-6.274							
14. TITLE (Provide with Security Classification Code)							
(U) Epidemiological Investigation of Dental Emergencies							
15. SCIENTIFIC AND TECHNOLOGICAL AREA							
012900 Physiology; 012600 Pharmacology; 003500 Clinical Medicine							
16. START DATE		17. REVISABLE COMPLETION DATE		18. FUNDING AGENCY		19. PERFORMANCE METHOD	
81 10		CONT		DA		C. IN-HOUSE	
20. CONTACT/STAFF				21. RESOURCES ESTIMATE		22. PROFESSIONAL MAN YRS	
23. DATE EFFECTIVE				24. FISCAL YEAR		25. FUND (in thousands)	
26. NUMBER				27. CURRENT		28. 75	
29. TYPE				30. AMOUNT		31. CUM. AMT.	
32. NAME OF AWARD				33. PERFORMANCE ORGANIZATION		34. SPECIAL INVESTIGATOR (Provide with U.S. Anatomic Pathology)	
35. NAME U.S. Army Institute of Dental Research				36. NAME U.S. Army Institute of Dental Research		37. NAME CARPENTER, W.M.	
38. ADDRESS Washington, DC 20307				39. ADDRESS Washington, DC 20307		40. TELEPHONE (202) 576-3258	
41. RESPONSIBLE INDIVIDUAL				42. SOCIAL SECURITY ACCOUNT NUMBER		43. POC: DA	
44. NAME SWEENEY, T.P.				45. NAME SHULMAN, J.		46. NAME GROVER, P.	
47. TELEPHONE (202) 576-3484				48. ADD: 17E INVESTIGATOR		49. ADD: 17E INVESTIGATOR	
50. GENERAL USE				51. GENERAL USE		52. GENERAL USE	
53. FOREIGN INTELLIGENCE CONSIDERED							
(U) Lip Pathology; (U) Herpetic Lesions; (U) Cold Weather Survey; (U) Xerocheilosis							
54. TECHNICAL OBJECTIVE, 55. APPROACH, 56. PROCESS (Provide detailed paragraphs identified by number. Provide in text of each with Security Classification Code.)							
<p>23. (U) To determine the causes of dental emergencies in a population of soldiers receiving regular dental care and to determine "at-risk-profiles" for those soldiers in critical occupation specialties so as to minimize problems with dental casualties during deployment.</p> <p>24. (U) Studies will be conducted among soldier populations to pinpoint the cause of dental emergencies, their frequency and diagnostic strategies which will permit the prediction of the potential of each soldier for such emergencies. The goal is to select out the "at-risk" group for dental treatment and thus minimize dental casualties during deployment.</p> <p>25. (U) (8210 - 8310) Analysis of data from the cold weather survey indicates that while actinic exposure is a risk factor in acute lip injury, relative humidity is even more significant. The modifying effects of complexion were also significant; in cold weather dark complexion is a risk factor, while it is a protective factor in hot weather. Based on these findings, the use of emollient preparations is recommended to protect the lips from dessication in a dry climate.</p>							

* Available to - enter here upon original's approval

DD FORM 1498

PREVIOUS EDITIONS OF THIS FORM ARE OBSOLETE. (FORMS 1498, 1 NOV 74)

PROJECT: 3S162775A825

WORK UNIT TITLE: (U) Epidemiological Investigation of Dental Emergencies

PRINCIPAL
INVESTIGATOR: COL William M. Carpenter, DC

The Prevalence of Lip Injury During
U. S. Army Cold Weather Exercises

PROBLEM: It is commonly assumed that extended outdoor exposure to extreme climates is a contributory cause of lip pathology, since the facial area is poorly protected from the environment. Soldiers on military operations are exposed to adverse climates to a greater degree than are civilians living in similar environments. They are often subjected to extreme physical exertion or long periods of minimal activity while exposed to an extremely cold environment. In cold weather for example, civilians spend, on the average, less than 5 to 10% of the day outdoors, while soldiers in the field spend 30% or more of the day outdoors. While acute lip problems are not medical emergencies, they are a morale problem for the troops. The prevalence and nature of cold weather lip damage has never been studied in a systematic manner. It was the purpose of this study to observe active duty soldiers engaged in cold-weather training and to document the prevalence of acute lip injury.

APPROACH: The studies were conducted at Fort Drum, New York. The first study occurred in January, 1980 during the "Empire Glacier" exercise. Participants were 763 personnel from Fort Bragg, North Carolina. The second study was conducted in January, 1982 during the "Snow Eagle" exercise. The participants were 659 personnel from Fort Campbell, Kentucky. Each survey was conducted during the third week of a four-week exercise. The subjects were interviewed and examined while they were waiting in mess hall lines. Each examination/interview for the purposes of this study took approximately 10-15 seconds. If lesions were found, a more thorough examination was performed. Data on the percentage of time devoted to outdoor duties were obtained by interview and were categorized as (a) more than 50% of time outdoors, (b) less than 50% outdoors, or (c) equal time outdoors and indoors. Age by decade and lip protectant use (Army issue; commercial, none) were elicited from the subjects. The presence of acute lip damage and type of complexion were also recorded during the examination. All examination data were agreed upon by both the examiner and the recorder.

RESULTS: Fifteen subjects (1.1%) exhibited severe acute lip damage; 743 (52.3%) exhibited moderate changes, and 664 (46.7%) had normal lips. Herpetic lesions were found in 32 (2.4%) of the 1331 soldiers included in the survey. The data on the frequency of acute lip injury during two field exercises were analyzed by age, use of lip protectant, complexion, amount of exposure, and weather. The association

between acute lip damage and age was not statistically significant in the sample. Eighty-five per cent of the study population was in the 17-29 age range. Dealing with a relatively small age range and recording age by decades, however, may have reduced the sensitivity of our study with regard to age as a risk factor. The hot-weather study dealt with a similar population. The prevalence of chronic lip damage was found to increase with age, but no information on age and frequency of acute lip damage was presented. The small number of females in our survey population (1.8%) did not justify stratification of the variables by sex. The association of acute lip injury with complexion was significant. Higher rates of acute lip damage were found in darker complected individuals. This finding was in conflict with the hot-weather survey. In dealing with a similar complexion distribution, both acute and chronic lip damage were found to vary significantly with complexion; with darker complexions having lower prevalence rates. A possible explanation for the conflicting results is that during the cold-weather surveys, the amount of actinic exposure was much less than that during the hot-weather survey. The amount of duty time spent outdoors was not significantly associated with the prevalence of lip injury. When the frequencies of acute lip damage in the two cold-weather surveys were compared (23% in 1982 and 12% in 1980), the differences were found to be significant. The weather during the second survey was colder, had less sun exposure, and resulted in an increased problem of lip damage. The relative humidity did not vary substantially during the two surveys. The modifying effects of complexion were significant; in cold weather, dark complexion is a risk factor, while it is a protective factor in hot weather. Age and amount of time spent outdoors are not significant risk factors in acute cold-weather lip injury.

PROJECT: 3S162775A825

WORK UNIT TITLE: (U) Natural History of Oral Lesions Encountered in the Soldier

PRINCIPAL
INVESTIGATOR: LTC Paul R. Burnett, DC

In Vitro Cytolytic Effects of Serum and Mononuclear
Leukocytes From RAS Patients

PROBLEM: Recurrent aphthous stomatitis (RAS), a stress-related condition prevalent in military populations, significantly impairs performance of duty of duty (in its more severe forms) and reportedly retards oral soft tissue wound healing. The objective of this research is to elucidate pathophysiological mechanisms responsible for the destruction of tissue and prolongation of healing associated with RAS.

APPROACH: A radioisotope-release assay utilizing trypsinized, ⁵¹Cr-labeled, allogeneic, nonkeratinizing oral epithelial cells has been developed to quantify immune cytotoxic activity in the serum and mononuclear leukocytes of RAS patients.

RESULTS: With approximately half of the necessary data gathered, the following trends are apparent:

1. Cytotoxic activity of fresh RAS sera exceeds that of matched control sera.
2. Cytotoxic activity of RAS mononuclear leukocytes is not significantly greater than matched controls.
3. In some cases, heat-inactivated RAS sera show significantly greater cytotoxic activity when combined with RAS (autologous) mononuclear leukocytes than with control leukocytes (during early stage of active disease, only).

Both complemented-mediated and cell-mediated antibody-dependent cytotoxicity are implicated in this system.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ACCESSION ¹	2. DATE OF SUMMARY ²	REPORT CONTROL SYMBOL DD-DHAE(AN)8JS	
3. DATE PREVIOUS ³	4. KIND OF SUMMARY	5. SUMMARY ICT ⁴	6. WORK SECURITY ⁵	7. ABRIDGMENT ⁶	8. ORIGIN INSTR ⁷	9. SPECIFIC DATA: CONTRACTOR ACCESS ⁸ <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	
82 10 01	D CHANGE	U	U		NL		
10. NO./CODES ⁹	PROGRAM ELEMENT	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER			
	62775A	3S162775A825	AA	007			
11. CONTINUING							
STOG 82/83-6.2/4							
12. TITLE (Pursuant to Security Classification Code) ¹⁰ (U) New and Improved Techniques for Grafts and Bone Regeneration in Traumatic Wounds							
13. SCIENTIFIC AND TECHNOLOGICAL AREA ¹¹							
012900 Physiology; 002400 Bioengineering; 002600 Biology							
14. START DATE		15. ESTIMATED COMPLETION DATE		16. FUNDING AGENCY		17. PERFORMANCE METHOD	
69 01		CONT		DA		C. IN-HOUSE	
18. CONTRACT/GRANT				19. RESOURCES ESTIMATE			
a. DATE/EFFECTIVE:				b. PRESENT			
c. NUMBER ¹²				d. PROFESSIONAL MAN YRS			
e. TYPE:				f. FUNDS (in thousands)			
g. KIND OF AWARD				h. CUM. AMT.			
10. RESPONSIBLE ORG ORGANIZATION				20. PERFORMING ORGANIZATION			
NAME ¹³ U.S. Army Institute of Dental Research				NAME ¹⁴ U.S. Army Institute of Dental Research			
ADDRESS ¹⁵ Washington, DC 20307				ADDRESS ¹⁶ Washington, DC 20307			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Pursuant to U.S. A. Contract (Continuation))			
NAME: SWEENEY, T.P.				NAME ¹⁷ HOLLINGER, J.O.			
TELEPHONE: (202) 576-3484				TELEPHONE: (202) 576-3764			
21. GENERAL USE				SOCIAL SECURITY ACCOUNT NUMBER POC:DA			
Foreign Intelligence Considered				ASSOCIATE INVESTIGATORS			
				NAME: WOODYARD, S.			
				NAME: O'NEAL, R.			
22. RESEARCH (Pursuant to Security Classification Code) (U) Tricalcium Phosphate; (U) Ceramic Block; (U) Segmental Mandibular Defects; (U) Granular Tricalcium Phosphate; (U) Laboratory Animals							
23. (U) Current methodologies for managing combat maxillofacial wounds and preventing/treating dental emergencies in the field will be extremely difficult to apply under the condition anticipated in future war. New methods are required which will permit more rapid definitive care, reduce morbidity and decrease logistic load. Thus the objective of this work unit is to develop simple, rapid methods for soft tissue or bone grating utilizable by the dental specialist in the field.							
24. (U) The fate, metabolism, osteogenic potential and tissue compatibility of ceramic and copolymer materials will be studied alone and in combination. The application of these and other materials to avulsive type wounds in both animals and humans will be pursued.							
25. (U) Due to loss of principal investigator and difficulties in the production of biodegradable, unidirectional porosity Tricalcium Phosphate (TCP), no significant progress has been made. A third generation TCP is in production and will be evaluated in experimental animals as soon as it becomes available. Implants of 50:50 Polylactic-Polyglycolic Acid (PLA/PGA) have been surgically inserted in five dogs. Two dogs have been sacrificed. The remaining surgery will be completed by Dec 1983. The remaining animals will be sacrificed by Dec 1983. Histologic preparation of the specimens and evaluation of results should be completed by June 1984.							

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				1. AGENCY ABBREVIATION	2. DATE OF SUMMARY	REPORT CONTROL SYMBOL	
				DA OK 6020	83 10 01	DD-DR&E(AR)35	
DATE PREVIOUS	3. CLASS OF SUMMARY	4. SUMMARY TYPE	5. WORK SECURITY	6. ABBREVIATION	7. ORG'S DESIGN	8. SPECIFIC DATA CONTRACTOR ACCESS	9. LEVEL OF WORK
82 10 01	D CHANGE	U	U		NI	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	A. WORK UNIT
NO./CODES	PROGRAM ELEMENT	PROJECT NUMBER	TACH AREA NUMBER		WORK UNIT NUMBER		
PRIMARY	62775A	3S1622775A825	AA		008		
CONTINUOUS							
TITLE (Provide with Security Classification Code)		STOG 82/83-6.2/4					
(U) Biodegradable Materials for the Treatment of Fractures and Soft Tissue Wounds in the Military Situation							
SCIENTIFIC AND TECHNOLOGICAL AREA							
012900 Physiology - 010300 Miscellaneous Materials							
10. ESTIMATED COSTS		11. FUNDING AGENCY		12. PERFORMANCE METHOD			
68 01		CONT		DA		C IN-HOUSE	
13. REQUIRED ESTIMATE		14. PROFESSIONAL MAN YRS		15. FUNDS (in thousands)			
PRELIMINARY		0.7		75			
83		0.7		83			
84		0.7		83			
16. PERFORMANCE ORGANIZATION							
NAME: USA Institute of Dental Research				NAME: USA Institute of Dental Research			
ADDRESS: Washington, DC 20307				ADDRESS: Washington, DC 20307			
PRINCIPAL INVESTIGATOR (Provide NAME, N.O., and degree (if necessary))				NAME: Hollinger, J.			
TELEPHONE: 202 576-3484				TELEPHONE: 202 576-3764			
SECURITY ACCOUNT NUMBER:				POC:DA			
ASSOCIATE INVESTIGATORS							
NAME:							
NAME:							
Foreign Intelligence Considered							
(U) Biodegradable Copolymer; (U) Tracheal Grafts (U) Diphosphoinositide-Lysosyme; (U) Laboratory Animals							
17. TECHNICAL OBJECTIVE, 18. APPROACH, 19. PROGRESS (Provide individual paragraphs identified by number, provide text of each with security classification code.)							
23. (U) To develop rapid and improved methods of treating combat injuries of the head and neck in the field using biodegradable materials. To develop premedicated biodegradable tissue fixation devices.							
24. (U) Biodegradable polylactic acid, polyglycolic acid and various combinations of these polymers as well as other polymers being developed will be applied in the development of surgical procedures for a variety of hard tissue, soft tissue and hollow organ injuries in animals and extended to man where appropriate.							
25. (U) Implant blocks have been inserted and evaluated in 8 dogs. By 7 months, implant-treated defects were completely healed. Implants for an additional 25 dogs were synthesized. Preparatory surgery has been performed on 3 animals. Biochemical and histochemical assays demonstrated suitable host response to the implant.							

PROJECT: 3S1622775A825
WORK UNIT TITLE: (U) Biodegradable Materials for the Treatment of
Fractures and Soft Tissue Wounds in the Military Situation
PRINCIPAL
INVESTIGATOR: LTC Jaffrey O. Hollinger, DC

A Study to Evaluate Copolymer of PLA:PGA and Diphosphoinositide-
Lysozyme for Bridging a Surgically Prepared Bone Discontinuity
Defect in Dogs

PROBLEM: Materials such as bone grafts and implants, collagen gels, ceramics, bone derivatives, and biopolymers are some of the many agents which have been employed for initiating osseous repair or for replacing bone. Failure rates ranging from 13% to greater than 30% have lead to a renewed interest in the development of more predictable compounds. A material was formulated, therefore, that consisted of the biopolymers PLA:PGA combined with a proteolipid (mucopeptide-N-acetylmuramolyhydro-lase:phosphatidyl inositol 4,5-diphosphate).

APPROACH: Two series of experiments were performed on a group of eight and a group of 25 adult mongrel dogs (mixed sexes, weighing 45-55 lbs). Selective, surgical extraction of teeth in ipsilateral arches was accomplished, and this preceded preparation of the host bed for receiving the implant. The implant was made by dissolving 50:50 PLA:PGA into methylene chloride and reprecipitating with anhydrous methanol. The proteolipid was added to this mixture which was placed into a Teflon mold. The mold was inserted into a vacuum oven at 50°C, 5 millitorr for 48 hours, followed by ethylene oxide sterilization. Host sites in the dogs' mandibles were prepared in the following manner: 1. Following 8 weeks of post-extraction healing, a 20mm segment was ablated, producing a complete discontinuity. This procedure was done on both sides of the mandibular arch. 2. A block of the implant of identical geometry to the defect was fabricated and was inserted into one defect. Stabilization and fixation were accomplished using ligature wire, a stainless steel plate, and stainless steel screws. 3. The contralateral defect was left untreated to serve as a control. All dogs were evaluated clinically at periodic intervals and lateral mandibular radiographs were taken.

RESULTS: The discontinuity defects in the mandibles of the group of 8 dogs that had been treated with the PLA:PGA-proteolipid implant developed an osseous union after six months. Bilateral palpation and manipulation of the mandible following removal of the internal fixation revealed complete stability. Radiographically, host-implant sites appeared within normal limits. The group of 25 dogs displayed results parallel to the group of 8 animals. Presently, histomorphometric and microdensitometric analyses of bone enzymes are underway. In both groups, complete tissue tolerance to the implant was demonstrated. Initial indications suggest that the PLA:PGA proteolipid may be useful for stimulating bony repair at intramembranous wound sites.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				DA301898	01 OCT 83	REPORT CONTROL SYMBOL Z01708
1. DATE OF REPORT 20 JUN 83	2. NAME OF REPORTING AGENCY A. NEW	3. REPORT TYPE U	4. DDD FORMATION U	5. SUBJECT	6. DISTRIBUTION STATEMENT NL	7. SOURCE DATA 71
10. NO./CODES 62778A	PROGRAM ELEMENT 3518277BA828	PROJECT NUMBER	TASK AREA NUMBER	WORK UNIT NUMBER		
PURPOSE MORDC ORJ. #Y00 : 82/83-G-2/8 :				D18		
(U) TUMORIGENICITY STUDY OF ISOBUTYL 2-CYANOACRYLATE						
O12800 PHYSIOLOGY		O18200 STRESS PHYS				
11. EFFECT DATE JUN 83	12. ESTIMATED EXECUTION DATE SEP 88	13. FUNDING AGENCY DA		14. PERFORMANCE METHOD C. IN-HOUSE		
15. DESCRIPTION				16. REFERENCES CITED		
a. BACKGROUND				b. PROFESSIONAL READ OUT		
c. SUMMARY				d. FUND ON REQUEST		
e. TYPE				f. COMMENTS		
g. KIND OF AWARD				h. OTHER INFORMATION		
F. CUM/TOT: 1 0				18. REFERENCES CITED		
NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR				NAME: MORDC INSTITUTE OF DENTAL RSCH USAIDR		
ADDRESS: WASHINGTON DC 20307				ADDRESS: WASHINGTON DC 20307		
RESPONSIBLE PERSONNEL				PERSONAL INVESTIGATOR		
NAME: SWEENEY, T P				NAME: CARPENTER, W M		
TELEPHONE: 202-878-3484				TELEPHONE: 202-876-3258		
17. SPECIAL USE				19. ADDRESS TO BE USED FOR CORRESPONDENCE		
P.I.C.A.				NAME: KOPPELMAN, E		
(U) ISOBUTYL 2-CYANOACRYLATE; (U) TUMORIGENICITY STUDY						
(U) LAB ANIMALS ;(U) TISSUE ADHESIVE ;(U) LIVER SURGERY ;(U) RATS ;(U) RAM IV;						
<p>OBJECTIVE: (U) ISOBUTYL 2-CYANOACRYLATE (ISC) HAS BEEN DEMONSTRATED TO BE AN EFFECTIVE TISSUE ADHESIVE FOR USE IN SUTURELESS WOUND CLOSURE. THE USE OF THIS MODALITY COULD PROVIDE A TIME SAVING AND SOMETIMES LIFE-SAVING DIMENSION TO THE MANAGEMENT OF COMBAT WOUNDS. THE PURPOSE OF THE PRESENT STUDY IS TO DETERMINE IF ANY TUMORIGENIC EFFECTS ARE PRODUCED BY THE LONG-TERM IMPLANTATION OF ISC.</p> <p>APPROACH: (U) THREE HUNDRED AND SIXTY ALBINO RATS WILL BE EQUALLY DIVIDED INTO A CONTROL AND EXPERIMENTAL GROUP; EACH GROUP CONTAINING EQUAL NUMBERS ACCORDING TO SEX. EACH ANIMAL WILL BE OPENED, THE LIVER EXPOSED AND EITHER TREATED WITH A THIN FILM OF ISC IN THE CASE OF THE EXPERIMENTALS OR SALINE IN THE CASE OF THE CONTROLS. THE INCISION WILL BE CLOSED AND ALL ANIMALS WILL BE MAINTAINED UNDER CAREFULLY CONTROLLED CONDITIONS. THE DURATION OF THE STUDY WILL BE TWO YEARS WITH HALF OF THE ANIMALS BEING SACRIFICED AT THE 364TH DAY. NECROPSIES WILL BE PERFORMED ON ALL ANIMALS AND HISTOLOGIC EXAMINATION UNDERTAKEN OF ALL ESSENTIAL TISSUES.</p> <p>PROGRESS: (U) NONE.</p>						

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				REPORT IDENTIFICATION		REPORT IDENTIFICATION SYMBOL	
DATE OF REPORT		TYPE OF REPORT		CLASSIFICATION		REPORT NUMBER	
				DA02071A		21 OCT 83 201708	
TO INCLUDE:		PROJECT NUMBER		TASK AREA NUMBER		WORK UNIT NUMBER	
PROGRAM ELEMENT		PROJECT NUMBER		TASK AREA NUMBER		WORK UNIT NUMBER	
82778A		29102778AA028		AA		DO	
(U) THE EFFECTIVENESS OF THE DENTAL RECORD IN THE IDENTIFICATION OF COMBAT CASUALTIES							
000400 ADMIN - MGT				008700 MATH STAT			
OCT 83				MAY 88			
C. IN-HOUSE				C. IN-HOUSE			
F. CHN/TOT.				S O			
038870				11			
MORDC INSTITUTE OF DENTAL RSCH USAIDR				MORDC INSTITUTE OF DENTAL RSCH USAIDR			
WASHINGTON DC 20307				WASHINGTON DC 20307			
NAME SWEENEY, Y P				NAME SHULMAN, J D			
TELEPHONE 202-678-2484				TELEPHONE 202-678-3520			
P.I.C.A.				BURNETT, P			
MILITARY				LEWIS, O			

OBJECTIVE: (U) TO DETERMINE THE RELIABILITY OF THE MILITARY DENTAL RECORD IN POSTMORTEM IDENTIFICATION OF A COMBAT CASUALTY.

APPROACH: (U) DENTAL IDENTIFICATION OF COMBAT CASUALTIES WILL BE SIMULATED USING AT LEAST 200 ACTIVE DUTY ARMY PATIENTS PRESENTING FOR ROUTINE EXAMINATIONS AT WALTER REED DENTAL CLINIC. SIMULATED ANTEORTHEM RECORDS (DENTAL RECORD AND RADIOGRAPHS) WILL BE DUPLICATED AND ASSIGNED A UNIQUE NUMBER. A SIMULATED POSTORTHEM RECORD WILL BE PREPARED SUBSEQUENT TO THE EXAMINATION. IT WILL CONSIST OF A ROUTINE DENTAL CHARTING AND DUPLICATES OF ANY RADIOGRAPHS ORDERED BY THE EXAMINING OFFICER. THE RECORD WILL ALSO BE ASSIGNED A UNIQUE NUMBER. A PANEL OF DENTAL OFFICERS WILL ATTEMPT TO MATCH THE SIMULATED ANTEORTHEM AND POSTORTHEM RECORDS. A LOGISTIC MODEL WILL BE CONSTRUCTED TO PREDICT THE PROBABILITY OF A CORRECT IDENTIFICATION AS A FUNCTION OF THE QUANTITY AND QUALITY OF THE INFORMATION IN THE SIMULATED ANTEORTHEM RECORD.

PROGRESS: (U) NONE.

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				REPORT CONTROL SYMBOL
DA202899		01 OCT 83		Z01708
A. NEW		U		A. WORK UNIT
PROGRAM ELEMENT		PROJECT NUMBER		WORK UNIT NUMBER
R2775A		25162778A828		011
TASK AREA NUMBER				
MISC OBJ SYOB : R2789-0 2/8 :				
(U) STORAGE STABILITY OF MEDICAL AND DENTAL MATERIALS				
012700 PHYS CHEM		008300 INORG CHEM		003500 CLIN MED
OCT 83	CONT		DA	C. IN-HOUSE
LABORATORY		F. CUM/TOT: 1 0		
MOADC INSTITUTE OF DENTAL RSCH USAIDR		WASHINGTON DC 20307		
WASHNEY, T P		MD 20		
202-876-3484		P.I.C.A.		
MILITARY		(U) STORAGE STABILITY ;(U) SHELF-LIFE ;(U) MEDICAL MATERIAL ;(U) DENTAL MATERIALS ;(U) RAM IV:		
OBJECTIVE:(U) MEDICAL AND DENTAL MATERIEL FOUND IN THE MILITARY LOGISTIC SYSTEM IS STORED IN SIX MAJOR DEPOTS WORLDWIDE. THE EXTREMES OF TEMPERATURE AND HUMIDITY CAN POTENTIALLY RENDER SOME OF THESE SUPPLIES INEFFECTIVE. ACCURATE SHELF-LIFE DATA ON POTENTIALLY PERISHABLE MEDICAL AND DENTAL MATERIEL IS VITAL TO INSURE THE VIABILITY OF SUPPLIES AFTER PERIODS OF STORAGE AND TRANSPORTATION.				
APPROACH: (U) BACKGROUND INFORMATION ON THE MILITARY LOGISTICS SYSTEM WILL BE STUDIED TO IDENTIFY POTENTIALLY PERISHABLE SUPPLIES, DETERMINE METHODS CURRENTLY USED FOR STORAGE AND IDENTIFY SPECIFICS OF ENVIRONMENTAL FACTORS TO WHICH MEDICAL AND DENTAL SUPPLIES ARE EXPOSED. THE SECOND PHASE OF THIS WORK WILL BE THE PHYSICAL TESTING OF IDENTIFIED MATERIEL AND THE DETERMINATION OF ACCURATE SHELF-LIFE DATA AFTER EXPOSURE TO AN ENVIRONMENTAL TESTING CHAMBER. THIS PROJECT WAS SLATED AS DA008033.				
PROGRESS: (U) NONE.				

DD 1400M

RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				PROJECT NUMBER DA302804		DATE OF REPORT 01 OCT 83		REPORT CONTROL NUMBER Z01708	
1. DATE OF REPORT A NEW		2. PROJECT/STUDY U		3. TITLE/STUDY U		4. PROJECT AREA CX		5. TYPE OF WORK A. WORK UNIT	
10. NO./CODES PROGRAM ELEMENT 81778A		PROJECT NUMBER 85182778A875		TASK AREA NUMBER AS		WORK UNIT NUMBER 623			
11. FUNDING WISS. OBJ. 5100 : 82/83-8378									
12. TITLE/STUDY (U) CLINICAL, RADIOGRAPHIC, AND HISTOLOGIC EVALUATION OF SERRATED CERAMIC TOOTH IMPLANTS									
13. SUBJECT/STUDY 0801 BIOCHEMISTRY		0808 CLIN MEDICINE		0818 PHYSIOLO					
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RESEARCH AND TECHNOLOGY WORK UNIT SUMMARY				REPORT CONTROL SYMBOL	
TO HQ/CODES =		PROJECT NUMBER		TASK AREA NUMBER	
PROGRAM ELEMENT		PROJECT NUMBER		WORK UNIT NUMBER	
82778A		35102778A28		024	
(U) SURFACE PHENOMENON OF OPAQUE PORCELAIN SUSPENSIONS ON OXIDIZED METAL					
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202-878-3484		415-581-5740		LORTON, L	
F.I.C.A.		MILITARY		MILITARY	
(U) MATERIALS : (U) DENTAL MATERIALS : (U) DENTAL PORCELAIN					

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A. PRIMARY	62734A	3M152734A875	AD	002			
B. CONTINUOUS							
C. DISCONTINUED	//////////	STOC 82/83-6 2/4					
12. TITLE (Precede with Security Classification Code)							
(U) Study of Saliva as a Diagnostic Tool for Presence of Lethal Agents							
13. IDENTIFYING AND TECHNOLOGICAL AREAS							
002300 Biochemistry 012600 Pharmacology - 012900 Physiology							
14. ENTRY DATE		15. ESTIMATED COMPLETION DATE		16. FUNDING AGENCY		17. PERFORMANCE METHOD	
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18. CONTRACT/GRANT				19. RESOURCES ESTIMATE		20. PROFESSIONAL MAN YRS	
A. DATE/EFFECTIVE				B. PRESENT		C. FUTURE (in Months)	
B. NUMBER				FISCAL YEAR		113	
C. TYPE				83		1.2	
D. KIND OF AWARD				84		1.0	
E. CUM. AMT.						122	
21. RESPONSIBLE DOD ORGANIZATION				22. PERFORMING ORGANIZATION			
NAME: USA Institute of Dental Research				NAME: USA Institute of Dental Research			
ADDRESS: Washington, DC 20307				ADDRESS: Washington, DC 20307			
RESPONSIBLE INDIVIDUAL				PRINCIPAL INVESTIGATOR (Precede with SSAN N.U.S. & include post-hoc)			
NAME: Sweeney, T.P.				NAME: Miller, R.A.			
TELEPHONE: 202 576-3484				TELEPHONE: 202-923-4915			
23. GENERAL USE				SOCIAL SECURITY ACCOUNT NUMBER: POC:DA			
				ASSOCIATE INVESTIGATORS			
				NAME: Setterstrom, J.A.			
				NAME:			
24. TECHNICAL OBJECTIVE, 25. APPROACH, 26. PROGRAM (Precede with individual paragraphs identified by number. Precede text of each with Security Classification Code)							
(U) Salivary Amylase; (U) Nerve Agent; (U) Salivary Physiology; (U) Salivary Enzyme; (U) Laboratory Animal (Rhesus Monkey)							
23. (U) To determine if saliva can be used as a diagnostic tool in evaluating the exposure of combat troops to chemical agents. To determine if constituents in saliva can be used to monitor the progress of therapy for chemical agent exposure. Develop a rapid, simplified field technique for diagnosis of chemical agent exposure in the combat soldier.							
24. (U) Changes in saliva produced by chemical agents and prophylactic antidotes will be evaluated. The particular areas of study will be enzyme, nucleotide, and protein components. Possible methodology developed will be evaluated in the field and at the hospital level.							
25. (U) (8210-8310) Previous work had suggested that variations in salivary amylase/total protein ratios may serve as the basis for the diagnosis of chemical agent exposure in the field. A new micro technique for the analysis of salivary cholinesterase has been developed. Salivary cholinesterase levels were determined for baseline and experimental salivary collections following exposure to the chemical agents and one of the prophylactic pretreatments. Work to date suggests that salivary cholinesterase may be useful for the diagnosis of nerve gas poisoning because organophosphates may be differentiated from the prophylactic levels of carbamates. Future work will examine enzyme levels of other agents and other carbamates as well as various combinations of each.							

PROJECT: 3S162775A825

WORK UNIT TITLE: A Study of Saliva as a Diagnostic Tool for Presence of Lethal Agents

PRINCIPAL INVESTIGATOR: Robert A. Miller

Study of Saliva as a Diagnostic Tool
for Presence of Lethal Agents

PROBLEM: One of the major concerns of the U. S. Army Medical Department is the survival of combat soldiers who have been exposed to chemical agents. In order to provide proper medical therapy, rapid diagnosis of nerve agents must be made. Presently, clinical signs are the basis of diagnosis of chemical agents in the field. The objective of this study was to determine if a biological parameter could be identified in saliva which could serve as the basis of a non-invasive method for the diagnosis of nerve gas poisoning in the combat soldier.

APPROACH: Biological parameters will be identified by monitoring changes in salivary composition produced by the organophosphate DFP (diisopropyl-fluorophosphate) and the prophylactic carbamates pyridostigmine, physostigmine and Mobam. Rhesus monkeys will be exposed to the anticholinesterases because of the biochemical similarity of its saliva to that of man. The particular parameters of study will be salivary flow rate, protein and the enzymes: cholinesterase, kallikrein, lysozyme, and amylase.

RESULTS: Work to date indicates that variations in salivary cholinesterase may serve as the basis for the diagnosis of chemical agent exposure. A radio-metric technique has been developed for the analysis of salivary cholinesterase. Salivary cholinesterase levels were determined for baseline and experimental collections following exposure to DFP and physostigmine. The results indicate that cholinesterase levels in saliva reflect blood cholinesterase levels following exposure to the organophosphate DFP. On the other hand, salivary cholinesterase levels were increased rather than inhibited like the blood cholinesterase levels following exposure to the carbamate physostigmine. Both physostigmine and DFP decreased salivary levels. They also increased the salivary levels of total protein, amylase, and lysozyme, but not significantly. The cholinergic drug physostigmine increased salivary flow rate. The organophosphate (DFP) caused a decrease in the rate of salivation which is in disagreement with previously reported signs of organophosphate poisoning.

Implications for Medical Defense Against Chemical Agents.

One of the characteristic clinical signs of nerve gas poisoning is increased salivation; however, this was not evident following exposure to 3/5 LD₅₀ dose of DFP. In fact, a decrease in flow rate was observed. This direct disagreement with previously reported characteristic signs of

organophosphate intoxication indirectly questions other reported signs of CW agent poisoning. Blood cholinesterase is the current clinical diagnostic procedure for organophosphate exposure. Findings to date suggest that using salivary cholinesterase for diagnosis of CW agent exposure is superior to the existing procedure because it can be used to differentiate organophosphate agents from the prophylactic carbamate pretreatment. In addition, a non-invasive technique can possibly be developed into a test strip for the soldier in the field.

USAIDR PUBLICATIONS

ABSTRACTS PRESENTED AT 1983 IADR MEETING

PUBLISHED IN THE JOURNAL OF DENTAL RESEARCH SPECIAL ISSUE A, 1983

G. L. Henley, J.C. Baumgartner*, and J.R. Wynkoop: Cytochemical Localization of Acetylcholine Esterase and Catecholamines In Injured Pulp.

M.L. Bryant*, J.O. Hollinger, and W.M. Carpenter: Computer Assisted Cytologic Assessment.

J.R. Wynkoop, R.A. Miller, N.F. Dalessandro*, A. Yancey, C. Mason, and J. VonBredow: Kallikrein and Flow-Rate Differences in Rhesus Saliva During Anesthesia.

M.A. Derevjaniuk*, J.A. Setterstrom, and L.N. Booker: Evaluation of Sporidicin and Cidex Following Clinical In-Use Conditions.

J.O. Hollinger, S.L. Finley*, and S.A. Gee: A Histomorphometric Assessment of PGE₂ Effect on Bone In Vitro.

P.S. Grover*, and J.O. Hollinger: Quantitative Assessment Comparing Scalpel and CO₂ laser Treatment of Soft Tissue Wounds.

J.R. Wynkoop, J.R. Heath*, R.A. Miller, N. Dalessandro, A. Yancey, and D. Mahon: Levels of Cyclic AMP in Rhesus Saliva After Anesthetic Injection.

G.L. Henley*, J.R. Wynkoop, and J.C. Baumgartner: Cytochemical Localization of Histamine and Dopamine in Injured Dental Pulp.

J.O. Hollinger: Histomorphometric Evaluation of Bone Healing at Endochondral and Intramembranous Sites.

J.R. Wynkoop, L. Kazyak*, R.A. Miller, and J.S. Harrington: Determination of Circulating Lidocaine Levels in Rabbits by GC/MS/DS.

J.R. Wynkoop, R.A. Miller*, N.F. Dalessandro, A.L. Yancey, J. VonBredow, and K. Lanza: Enzyme Activities and Proteins in Rhesus Saliva Following Anesthetic Injections.

R.A. Miller, J.R. Wynkoop, J.D. Shulman*, N.F. Dalessandro, K. Johannsen, and W.C. Cole: Chemical Parameters of Rhesus Saliva Following Diisopropyl Fluorophosphate.

J.O. Hollinger, J.J. Tamura, Jr.*, and S.A. Gee: Integration of Bone Histomorphometry and Histochemical Analyses.

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